Epidemiology of *Chlamydia trachomatis* in the Middle East and north Africa: a systematic review, meta-analysis, and meta-regression

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Summary

Background The epidemiology of *Chlamydia trachomatis* in the Middle East and north Africa is poorly understood. We aimed to provide a comprehensive epidemiological assessment of *C trachomatis* infection in the Middle East and north Africa.

Methods We did a systematic review of *C trachomatis* infection as well as a meta-analysis and meta-regression of *C trachomatis* prevalence. We searched PubMed and Embase, as well as regional and national databases up to March 13, 2019, using broad search terms with no language or year restrictions. Any document or report including biological measures for *C trachomatis* prevalence or incidence was eligible for inclusion. We extracted all measures of current (genital or rectal), recent, and ever infection with *C trachomatis*. We estimated pooled average prevalence in different populations using random-effects meta-analysis. Factors associated with prevalence and sources of between-study heterogeneity were determined using meta-regression.

Findings We identified a total of 1531 citations, of which 255 reports contributed to 552 *C trachomatis* prevalence measures from 20 countries. No incidence measures were identified. Pooled prevalence of current genital infection was 3·0% (95% CI 2·3–3·8) in general populations, 2·8% (1·0–5·2) in intermediate-risk populations, 13·2% (7·2–20·7) in female sex workers, 11·3% (9·0–13·7) in infertility clinic attendees, 12·4% (7·9–17·7) in women with miscarriage, 12·4% (9·4–15·7) in symptomatic women, and 17·4% (12·5–22·8) in symptomatic men. Pooled prevalence of current rectal infection was 7·7% (4·2–12·0) in men who have sex with men. Substantial between-study heterogeneity was found. Multivariable meta-regression explained 29·0% of variation. Population type was most strongly associated with prevalence. Additional associations were found with assay type, sample size, country, and sex, but not with sampling methodology or response rate (about 90% of studies used convenience sampling and >75% had unclear response rate). There was no evidence for temporal variation in prevalence between 1982 and 2018.

Interpretation *C trachomatis* prevalence in the Middle East and north Africa is similar to other regions, but higher than expected given its sexually conservative norms. High prevalence in infertility clinic attendees and in women with miscarriage suggests a potential role for *C trachomatis* in poor reproductive health outcomes in this region.

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Introduction

With more than 100 million incident infections every year,[1] *Chlamydia trachomatis* is one of the most common sexually transmitted infections (STIs) worldwide.[2,3] Although curable, control and early detection of *C trachomatis* infection are challenged by its largely asymptomatic nature.[4] Untreated *C trachomatis* infection is associated with serious reproductive tract conditions including pelvic inflammatory disease, ectopic pregnancy, infertility among women, and epididymitis among men.[5,6]

Despite burdensome sequelae, STI control has long languished on health policy agendas. The 2030 Agenda on Sustainable Development[7] aims to remedy this situation and led to WHO's Global Health Sector Strategy on STIs.[8] The strategy proposes an integrated approach for STI prevention and control that addresses core Sustainable Development Goals, mainly through securing universal access to sexual and reproductive health-care services and rights.[7,8] The first strategic direction of this STI Strategy is "the need to understand the sexually transmitted infection epidemic and response as a basis for advocacy, political commitment, national planning, resource mobilization and allocation, implementation, and programme improvement."[8]

The epidemiology of STIs, including *C trachomatis*, remains poorly understood in the Middle East and north Africa—a region comprising 10% of the world's population.[9–11] Here, political and sociocultural sensitivities have set STIs low on countries' public health agendas, resulting in limited capacity for surveillance and programmes targeting sexual health, despite the possibility of a hidden disease burden.[9] For example, the prevalence of primary infertility in the Middle East and north Africa, based on demographic and reproductive health surveys, has been

Research in context

Evidence before this study

In a context of continuing stigma and political and sociocultural sensitivities, the Middle East and north Africa region has a dearth of epidemiological data about sexually transmitted infections. The prevalence of *Chlamydia trachomatis* and its distribution among populations at differing levels of risk of exposure remain largely unknown. A PubMed search using the search criteria ("Chlamydia"[MeSH] AND "Review" [Publication Type]) identified no systematic review and meta-analysis of regional scope for all subpopulations for this infection in the Middle East and north Africa or elsewhere.

Added value of this study

Using rigorous state-of-the-art methodologies with current empirical evidence, this study provided the first comprehensive epidemiological assessment of *C trachomatis* infection in the Middle East and north Africa. The study searched diverse sources of data, beyond international electronic databases, and identified a large volume of published and unpublished data, some of which now appears in the literature for the first time. The scope of evidence allowed analyses that found revealing associations relevant for the Middle East and north Africa and elsewhere. Unexpectedly, given this region's sexually conservative norms, the study estimated a *C trachomatis* prevalence of 3% in the population at large, similar to estimates from other regions. The study also documented high *C trachomatis* prevalence levels in infertility clinic attendees and in women with miscarriage, with odds of infection three-times higher than in the general population.

Implications of all the available evidence

There is a substantial *C trachomatis* infection and disease burden in the Middle East and north Africa that is neglected and poorly recognised despite its social and economic toll in a region comprising 10% of the world's population. *C trachomatis* infection appears to be consistently associated with infertility and poor reproductive health outcomes in this region, yet these conditions are not linked to the possibility of an underlying infectious cause. The Middle East and north Africa is far from achieving WHO's Global Health Sector Strategy on Sexually Transmitted Infections, 2016–21. The findings of this study provide a scientific foundation to develop an evidence-informed public health response against *C trachomatis* and its burdensome sequelae. The challenge will be to implement effective targeted, culturally appropriate, and gender-specific programmes to tackle *C trachomatis* infection and improve sexual health in general.

estimated to be the highest worldwide (although that of secondary infertility seems to be the lowest).[12] Still, the contribution of *C trachomatis*, or other STIs, to this disease burden remains unknown. Against this background, our study aimed to characterise *C trachomatis* epidemiology in the Middle East and north Africa.

Methods

Search strategy and selection criteria

We did a systematic review as well as a meta-analysis and meta-regression. We followed systematic review methods proposed by the Cochrane Collaboration,[13] and report findings following the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines[14] (appendix pp 5–6). We did exhaustive searches using PubMed and Embase, regional and national databases (WHO Index Medicus for the Eastern Mediterranean region, Iraqi Academic Scientific Journals database, and Iranian Scientific Information Database), abstract archives of International AIDS Society Conferences,[15] as well as country-level and international organisations' reports available through the Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project database.[10,11]

See Online for appendix

Our searches were done up to March 13, 2019, using broad search terms (MeSH/Emtree terms exploded to cover all subheadings and free-text terms) with no language or year restrictions. The appendix (p 7) summarises the search criteria and search terms used. The Middle East and north Africa were defined as 23 countries extending from Morocco in the west to Pakistan in the east (appendix p 8). This definition for the Middle East and north Africa follows earlier convention applied in HIV and hepatitis C research,[10,16–22] and is based on definitions by WHO, UNAIDS, and the World Bank.

Search results were checked for duplicates using Endnote (version 8.2). We screened titles and abstracts of unique citations. Full texts of citations deemed relevant or potentially relevant were retrieved for further screening by AS and HC. Any document or report including biological measures for *C trachomatis* prevalence or incidence, or both, based on primary data was eligible for inclusion. Case reports, case series, editorials, commentaries, reviews, and reports about military personnel stationed in the Middle East and north Africa, but not from these countries, were excluded. Reference lists of literature reviews and all relevant articles were hand-searched for additional eligible reports.

In this Article, the term report refers to a document (article, conference abstract, or country-level report) containing outcome measures of interest (ie, prevalence or incidence) for one or more populations, and the term study refers to details of a specific outcome measure in a specific population. Consequently, one report could contribute multiple studies and one study could be published in different reports. Duplicate study results were included only once using the most detailed report.

Data analysis

Data from relevant reports were extracted by AS with input from LJA-R. Independent extraction was done by

HC, and discrepancies were settled by consensus, or by contacting authors. Data from non-English articles were extracted from the full text by native speakers.

We extracted all measures of current (genital or rectal), recent, and ever infection with *C trachomatis*. We stratified data according to the study population's risk of exposure to *C trachomatis* or clinical manifestations (panel). Populations were defined as per original study authors' specific population definition and inclusion criteria (such as for infertile populations or women with miscarriage). We classified women and men as symptomatic only if there was an indication for the presence of *C trachomatis*-related signs and symptoms. We subsequently synthesised data by type of assay used for *C trachomatis* detection and summarised these data using medians and ranges.

Studies applying the same assay to different biological specimens were included only once, based on a sequential order that prioritised, for women, *C trachomatis* detection in endocervical swabs, followed by vaginal and urine samples; and for men, detection in urethral swabs, followed by urine and semen samples. Studies applying nucleic acid amplification test (NAAT) and culture to the same biological specimen were included separately given our interest in studying their contribution to heterogeneity in *C trachomatis* prevalence, and in generating STI-estimation correction factors based on assay type.[23–25] Studies applying other antigen detection assays to the same biological specimen were included only once based on assay sensitivity (direct fluorescence and enzyme-linked immunoassays on genital samples were prioritised over Giemsa staining).

We excluded studies using tissue specimens from the upper genital tract, or including less than ten participants. We stratified the analyses by sex where relevant. Studies reporting only an overall measure for men and women were classified according to the predominant sex in the sample.

We did risk of bias and precision assessments. Informed by the Cochrane approach,[13] we classified studies as having low versus high risk of bias for each of three quality domains assessing rigour of sampling methodology (probability based *vs* non-probability based), type of *C trachomatis* ascertainment (biological assay *vs* other, such as self-report), and response rate (≥80% response rate or ≥80% of target sample size reached [the latter for studies using respondent-driven sampling] *vs* <80%). Studies with unavailable information about any given domain were classified as having unclear risk of bias for that domain. Studies were considered of higher precision if 200 participants or more underwent testing for *C trachomatis*, which was judged as an acceptable level of precision assuming a mean prevalence of 3% in the general population.

We produced forest plots to visualise estimates of prevalence and 95% CIs for each at-risk population, stratified by type of assay. Pooled average prevalence and 95% CIs were then estimated using meta-analysis for each stratum. A Freeman-Tukey type arcsine square-root transformation was first applied to stabilise variances of prevalence measures.[26,27] Measures were then weighted using the inverse-variance method,[27,28] before being pooled using a DerSimonian-Laird random-effects model.[29] This model assumes a normal distribution for true effect sizes (ie, prevalence) across studies, which factors in sampling variation and true between-study heterogeneity.[30]

We did heterogeneity assessment using Cochran's Q statistic to confirm existence of heterogeneity across studies, I^2 to quantify magnitude of between-study variation that is due to true differences in effect size rather than chance, and prediction interval to estimate the 95% CI of the distribution of true effect sizes.[30,31] We did subgroup meta-analyses whenever five studies or more were available, using the R software (version 3.4.2).[32]

We did random-effects meta-regression analyses to identify sources of between-study heterogeneity and estimated the magnitude of their association with prevalence. We included risk of bias and precision domains in the meta-regression analyses. We considered the

***Panel:* Definitions for at-risk population classification**

General populations (populations at low risk)
Populations at low risk of exposure to *Chlamydia trachomatis* infection such as antenatal clinic attendees, blood donors, and pregnant women.

Populations at intermediate risk
Populations who presumably might have some sexual contacts with populations engaging in high sexual risk behaviour, and have therefore a higher risk of exposure to *C trachomatis* than the general population. These populations comprise prisoners, people who inject drugs, truck drivers, migrant workers, and HIV-infected individuals in a setting where the HIV epidemic is driven by injecting drug use.

Populations at high risk
Populations at high risk of exposure to *C trachomatis* as a consequence of specific high sexual risk behaviours such as female sex workers, men who have sex with men, male sex workers, men-to-women transgenders, and HIV-infected individuals in a setting where the HIV epidemic is driven by sexual transmission.

Infertility clinic attendees
Infertile women or men and their partners were included in a separate category given the potential biological link between *C trachomatis* infection and infertility.

Women with miscarriage
These women were included in a separate category given the potential biological link between *C trachomatis* infection and miscarriage.

Women with ectopic pregnancy
These women were included in a separate category given the potential biological link between *C trachomatis* infection and ectopic pregnancy.

Symptomatic women
Women with clinical manifestations related to *C trachomatis* infection, or suspected of having a *C trachomatis* infection such as those with vaginal discharge.

Symptomatic men
Men with clinical manifestations related to *C trachomatis* infection, or suspected of having a *C trachomatis* infection such as those with urethral discharge.

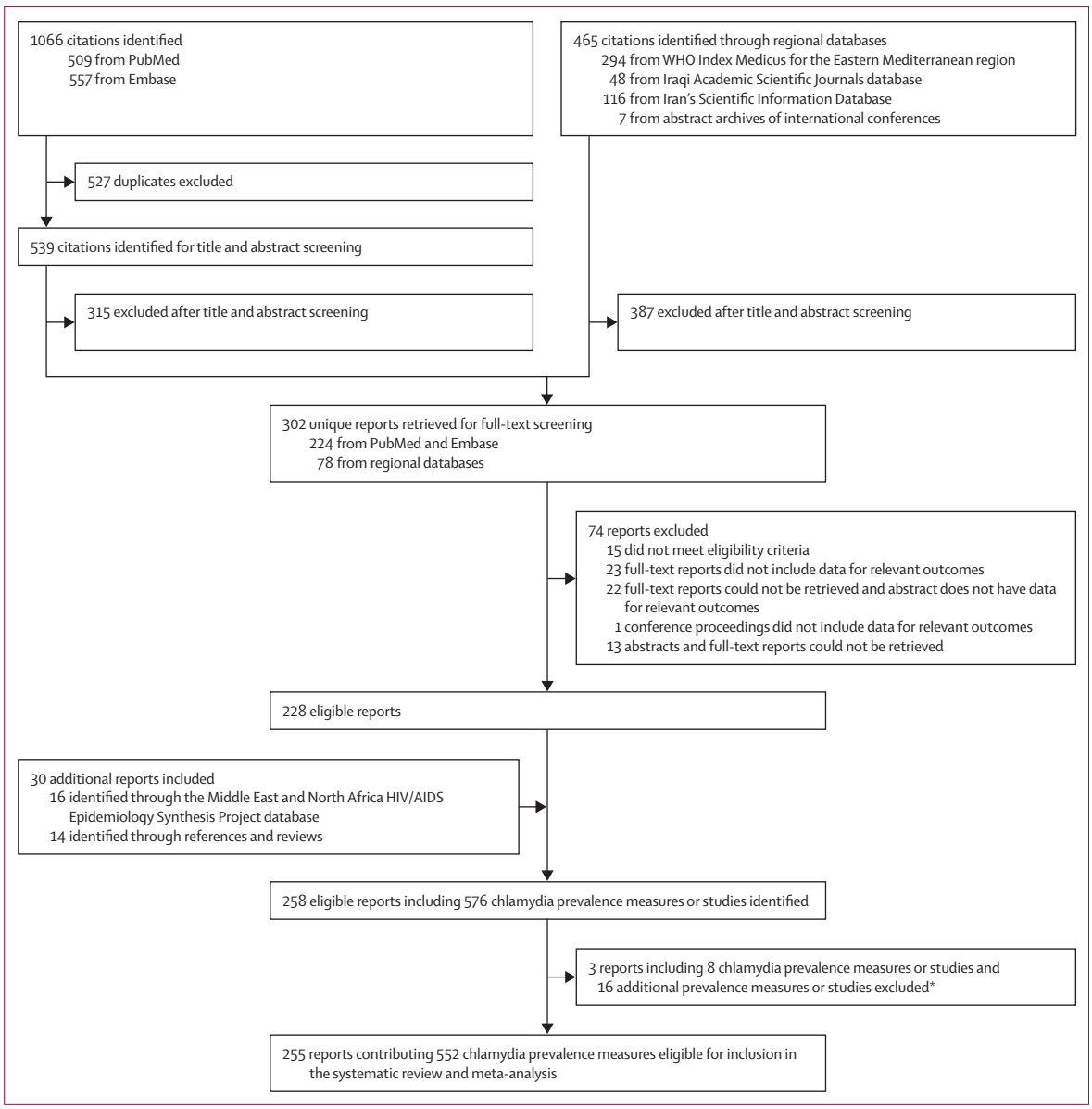

Figure 1: **Flow chart of the study selection process for the systematic review**
The systematic review focused on *Chlamydia trachomatis* incidence or prevalence, or both, in the Middle East and north Africa. *Reasons for exclusion: 14 studies applied the same assay to different biological specimens, and prevalence was included only once based on a sequential order prioritising for women *C trachomatis* detection in endocervical swabs followed by vaginal and urine samples, and for men detection in urethral swabs followed by urine and semen samples; one study applied antigen detection assays (other than nucleic acid amplification assays and culture) to the same biological specimen, and prevalence was included only once based on assay sensitivity; two studies were conducted only on subsamples of an original sample, and the prevalence in the original sample was included in the systematic review; six studies and three reports used tissue specimens from the upper genital tract; and one study had a sample size of less than 10.

following predictors a priori: at-risk population (panel), assay type (NAAT, culture, other assays detecting current infection, serological assays detecting anti-*C trachomatis* immunoglobulins of class IgG, IgM, IgA, immunoglobulins not specified, and unclear), sampling methodology (non-probability-based sampling *vs* probability-based sampling), sample size (<200 *vs* ≥200 participants), response rate (≥80% *vs* <80% and unclear), year of publication, year of data collection, country (Egypt, Iran, Pakistan, and remaining countries; Egypt, Iran, and Pakistan being the most populous in the Middle East and north Africa),[33] and sex (women *vs* men; men-to-women transgenders who were biologically males were considered as men).

Studies that assessed *C trachomatis* prevalence using different diagnostics or biomarkers were included independently. Missing values for year of data collection were imputed using data for year of publication adjusted

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
Kadi et al (1990)[35]	Algeria	Cross-sectional	Convenience	69	W	Gynaecology clinic	Gynaecology clinic attendees	Serum	MIF (IgG)	17·4%
Kadi et al (1990)[35]	Algeria	Cross-sectional	Simple random sampling	180	W	Hospital	Women seeking rubella tests	Serum	MIF (IgG)	26·6%
Abdel Monem et al (2005)[36]	Egypt	Case-control	Convenience	20	W	Antenatal clinic	Pregnant women	Endocervical	Culture	15%
Aboul Atta and Ibrahem (1995)[37]	Egypt	Case-control	Convenience	20	M	Hospital	Controls in STI study	Urethral	DFA	5%
Badary (1996)[38]	Egypt	Case-control	Convenience	32	W	Gynaecology clinic	Fertile women	Endocervical	DFA	12·5%
Berry and El Shabrawy (1996)[39]	Egypt	Case-control	Convenience	30	W	Family planning clinic	Family planning clinic attendees	Serum	EIA (IgG)	3·3%
Diab (1993)[40]	Egypt	Case-control	Convenience	30	W	Antenatal clinic	Women with full-term delivery	Serum	EIA (IgG)	0
Draz et al (2018)[41]	Egypt	Case-control	Convenience	14	W	Gynaecology clinic	Healthy women	Endocervical	DFA	0
El-Sayed et al (2002)[42]	Egypt	Cross-sectional	Convenience	108	W	Family planning clinic	Family planning clinic attendees	Urine	NAAT	2·8%
El-Sayed et al (2002)[42]	Egypt	Cross-sectional	Convenience	604	W	Antenatal clinic	Antenatal clinic attendees	Urine	NAAT	1·3%
Mosbah and Nabiel (2016)[43]	Egypt	Case-control	Convenience	90	W	Hospital	Pregnant women with pre-eclampsia	Endocervical	NAAT	4·4%
Mosbah and Nabiel (2016)[43]	Egypt	Case-control	Convenience	90	W	Hospital	Normotensive pregnant women	Endocervical	NAAT	0
Mousa (1990)[44]	Egypt	Cross-sectional	Convenience	50	W	Gynaecology clinic	Gynaecology clinic attendees	Endocervical	DFA	2%
Nada et al (2015)[45]	Egypt	Case-control	Convenience	100	W	Gynaecology clinic	Gynaecology clinic attendees	Endocervical	NAAT	2%
Sullam et al (2001)[46]	Egypt	Cross-sectional	Multistage cluster sampling	1344	W	Community	Household survey of women	Endocervical	ELISA	4·2%
Zaki (1989)[47]	Egypt	Cross-sectional	Convenience	100	W	Antenatal clinic	Pregnant women	Endocervical	Culture	3%
Ahmadi et al (2016a)[48]	Iran	Case-control	Convenience	109	W	Family planning clinic	Family planning clinic attendees	Endocervical	NAAT	11·9%
Ahmadi et al (2018)[49]	Iran	Case-control	Convenience	165	M	Clinic	Fertile men	Semen	NAAT	0·6%
Ahmadnia et al (2016)[50]	Iran	Cross-sectional	Stratified cluster sampling	4274	W	Primary health-care centre	Primary health-care centre clinic attendees	Endocervical	Culture	1%
Badami and Salari (2001)[51]	Iran	Cross-sectional	Convenience	250	W	Family planning clinic	Family planning clinic attendees	Serum	DFA	0·8%
Badami and Salari (2001)[51]	Iran	Cross-sectional	Convenience	250	W	Family planning clinic	Family planning clinic attendees	Serum	Unclear	3·2%
Baghchesaraei et al (2011)[52]	Iran	Cross-sectional	Convenience	328	W	Gynaecology clinic	Gynaecology clinic attendees	Serum	EIA (IgM)	10·3%
Bagheri et al (2018)[53]	Iran	Case-control	Convenience	60	W	Fertility centre	Pregnant women	Vaginal	NAAT	0
Bagheri et al (2018)[53]	Iran	Case-control	Convenience	60	W	Fertility centre	Pregnant women	Serum	ELISA (IgA)	6·7%
Bagheri et al (2018)[53]	Iran	Case-control	Convenience	60	W	Fertility centre	Pregnant women	Serum	ELISA (IgG)	1·7%
Behroozi (2001)[54]	Iran	Cross-sectional	Convenience	400	W	Antenatal clinic	Pregnant women	Unclear	DFA	2·8%
Chamani-Tabriz et al (2008)[55]	Iran	Cross-sectional	Convenience	991	W	Community	Married women	Urine	NAAT	12·8%
Cheraghi et al (2014)[56]	Iran	Cross-sectional	Convenience	1448	W	Health centres	Non-pregnant women	Endocervical	Unclear	0·2%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Antenatal clinic	Antenatal clinic attendees	Urine	NAAT	0
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Antenatal clinic	Antenatal clinic attendees	Serum	EIA (IgA)	0
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Antenatal clinic	Antenatal clinic attendees	Serum	EIA (IgM)	0
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Antenatal clinic	Antenatal clinic attendees	Serum	EIA (IgG)	12·8%
Goshayeshi et al (2015)[58]	Iran	Case-control	Convenience	30	W	Fertility centre	Fertile women	Endocervical	NAAT	3·3%
Haghighi Hasanabad et al (2013)[59]	Iran	Cross-sectional	Convenience	399	W	Antenatal clinic	Pregnant adolescents	Unclear	NAAT	12·3%
Jahromi et al (2010)[60]	Iran	Case-control	Convenience	200	W	Gynaecology clinic	Women with full-term delivery	Endocervical	DFA	5·2%
Javanmard et al (2018)[61]	Iran	Cross-sectional	Convenience	210	W	Gynaecology clinic	Women undergoing routine pap smear	Endocervical	NAAT	11·4%

(Table 1 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	125	W	Hospital	Pregnant women	Vaginal	NAAT	1·6%
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	125	W	Hospital	Pregnant women	Serum	ELISA (IgM)	1·6%
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	125	W	Hospital	Pregnant women	Serum	ELISA (IgG)	0
Kajbaf and Gholamnezhad (1998)[63]	Iran	Case-control	Convenience	50	W	Antenatal clinic	Antenatal clinic attendees	Endocervical	DFA	4%
Kajbaf and Gholamnezhad (1998)[63]	Iran	Case-control	Convenience	50	W	Antenatal clinic	Antenatal clinic attendees	Serum	ELISA (IgG)	6%
Kamyabi (2009)[64]	Iran	Case-control	Convenience	35	W	Gynaecology clinic	Pregnant women	Serum	ELISA (IgG)	20%
Khezerdoust et al (2009)[65]	Iran	Cross-sectional	Convenience	1114	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgG)	2·9%
Marashi et al (2014)[66]	Iran	Case-control	Convenience	200	W	Antenatal clinic	Pregnant women	Endocervical	DFA	3·5%
Marashi et al (2014)[66]	Iran	Case-control	Convenience	200	W	Antenatal clinic	Pregnant women	Endocervical	NAAT	8·7%
Ministry of Health and Medical Education (2008)[67]	Iran	Case-control	Convenience	41	W	Clinic	Fertile women	Serum	ELISA (IgG)	2·4%
Meidani (2009)[68]	Iran	Cross-sectional	Simple random sampling	140	M	Laboratory	Men—premarital or pre-employment screening	Urine	NAAT	0·7%
Ministry of Health and Medical Education (2008)[67]	Iran	Cross-sectional	Convenience	70	W	Antenatal clinic	Pregnant women	Serum	ELISA (unclear)	4·3%
Ministry of Health and Medical Education (2008)[67]	Iran	Case-control	Convenience	250	W	Family planning clinic	Healthy women	Endocervical	DFA	0·8%
Mousavi et al (2014)[69]	Iran	Case-control	Convenience	104	W	Antenatal clinic	Antenatal clinic attendees	Endocervical	NAAT	5·8%
Pourabbas et al (2018)[70]	Iran	Cross-sectional	Convenience	239	W	Hospital	Pregnant women	Endocervical	NAAT	15·5%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	223	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgM)	1·8%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	223	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgG)	5·0%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	223	W	Antenatal clinic	Pregnant women	Urine	NAAT	8·5%
Rohi et al (2011)[72]	Iran	Cross-sectional	Convenience	91	W	Hospital	Pregnant women	Serum	ELISA (IgG)	28·6%
Rostami et al (2016)[73]	Iran	Cross-sectional	Simple random sampling	518	W	Gynaecology clinic	Gynaecology clinic attendees	Endocervical	NAAT	7·1%
Safdari et al (2015)[74]	Iran	Cross-sectional	Convenience	70	W	Antenatal clinic	Antenatal clinic attendees	Endocervical	NAAT	10%
Safdari et al (2015)[74]	Iran	Cross-sectional	Convenience	70	W	Antenatal clinic	Antenatal clinic attendees	Endocervical	Culture	8·6%
Sattari et al (2017)[75]	Iran	Case-control	Convenience	100	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgM)	2%
Sattari et al (2017)[75]	Iran	Case-control	Convenience	100	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgG)	18%
Sisakht et al (2017)[76]	Iran	Case-control	Convenience	30	W	Gynaecology clinic	Women with full-term delivery	Urine	NAAT	4·7%
Yeganeh et al (2013)[77]	Iran	Case-control	Convenience	100	M	Urology clinic	Asymptomatic men	Urine	NAAT	4%
Zahirnia et al (2018)[78]	Iran	Cross-sectional	Convenience	76	W	Gynaecology clinic	Pregnant women	Vaginal	NAAT	10·5%
Abdulkhudher et al (2014)[79]	Iraq	Case-control	Convenience	40	W	Antenatal clinic	Women with full-term delivery	Serum	ELISA (IgM)	0
Abdulkhudher et al (2014)[79]	Iraq	Case-control	Convenience	40	W	Antenatal clinic	Women with full-term delivery	Serum	ELISA (IgG)	7·5%
Abdul-Karim et al (2009)[80]	Iraq	Cross-sectional	Convenience	198	W	Hospital	Women with full-term delivery	Serum	ELISA (IgG)	13·7%
Abdullah (2012)[81]	Iraq	Case-control	Convenience	24	W	Hospital	Pregnant women	Serum	ELISA (IgM)	0
Abdullah (2012)[81]	Iraq	Case-control	Convenience	24	W	Hospital	Pregnant women	Serum	ELISA (IgG)	8·3%
Ahmed (2008)[82]	Iraq	Case-control	Convenience	30	W	Hospital	Women with full-term delivery	Serum	ELISA (unclear)	0
Al-Hamdani et al (2010)[83]	Iraq	Case-control	Convenience	17	W	Hospital	Pregnant women	Serum	ELISA (IgM)	14·0%

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	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Al-Hamdani et al (2010)[83]	Iraq	Case-control	Convenience	17	W	Hospital	Pregnant women	Serum	ELISA (IgG)	14·0%
Al-Hamdani et al (2010)[83]	Iraq	Case-control	Convenience	17	W	Hospital	Pregnant women	Serum	ELISA (IgA)	40·4%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	100	W	Family planning clinic	Family planning clinic attendees	Serum	IFAT (unclear)	5%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	100	W	Family planning clinic	Family planning clinic attendees	Endocervical	ELFA	4%
Ali and Al-Kazaz (2018)[85]	Iraq	Case-control	Convenience	13	M	Clinic	Fertile men	Semen	NAAT	0
Alkhafaf (2013)[86]	Iraq	Case-control	Convenience	122	W	Hospital	Married women	Serum	ELISA (IgG)	4·1%
Alkhafaf (2013)[86]	Iraq	Case-control	Convenience	168	W	Hospital	Unmarried woman	Serum	ELISA (IgG)	2·4%
Hwaid et al (2013)[87]	Iraq	Case-control	Simple random sampling	91	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgG)	5·5%
Hwaid et al (2013)[87]	Iraq	Case-control	Simple random sampling	91	W	Antenatal clinic	Pregnant women	Serum	ELISA (IgM)	3·3%
Ismail and Ali (2012)[88]	Iraq	Case-control	Convenience	50	W	Laboratories	General population women	Serum	ELISA (IgM)	10%
Ismail and Ali (2012)[88]	Iraq	Case-control	Convenience	50	W	Laboratories	General population women	Serum	ELISA (IgG)	4%
Ismail and Ali (2012)[88]	Iraq	Case-control	Convenience	50	W	Laboratories	General population women	Serum	ELISA (IgA)	2%
Mohammed et al (2012)[89]	Iraq	Case-control	Convenience	23	W	Gynaecology clinic	Pregnant women	Serum	ELISA (IgM)	0
Mohammed et al (2017)[90]	Iraq	Case-control	Convenience	20	W	Gynaecology clinic	Gynaecology clinic attendees	Endocervical	NAAT	0
Mohammed et al (2017)[90]	Iraq	Case-control	Convenience	20	W	Gynaecology clinic	Gynaecology clinic attendees	Serum	ELISA (IgG)	0
Yahya and Al-Siraj (2009)[91]	Iraq	Cross-sectional	Convenience	296	M	Laboratory	Fertile men	Serum	Culture	0
Abusarah et al (2013)[92]	Jordan	Case-control	Convenience	61	M	Urology clinics	Fertile men	Urine	NAAT	1·6%
Al-Ramahi et al (2008)[93]	Jordan	Case-control	Convenience	146	W	Gynaecology clinic	Gynaecology clinic attendees	Endocervical	NAAT	0·7%
As'ad (2004)[94]	Jordan	Cross-sectional	Convenience	144	W	Family planning clinic	Asymptomatic women	Vaginal	NAAT	0
Awwad et al (2003)[95]	Jordan	Case-control	Convenience	61	M	Urology clinic	Non-urethritis patients	Urine	NAAT	0
Awwad et al (2003)[95]	Jordan	Case-control	Convenience	39	W	Urology clinic	Non-urethritis patients	Urine	NAAT	0
Mahafzah et al (2008)[96]	Jordan	Cross-sectional	Convenience	186	W	Gynaecology clinic	Family planning clinic attendees	Endocervical	NAAT	0·5%
Jordan Ministry of Health (2004)[97]	Jordan	Cross-sectional	Convenience	213	W	Hospital	Asymptomatic women	Endocervical	NAAT	0·5%
Al-Awadhi et al (2018)[98]	Kuwait	Cross-sectional	Convenience	65 338	W	Laboratory	Women undergoing pap smear 1997–2005	Endocervical	Unclear	0·1%
Al-Awadhi et al (2018)[98]	Kuwait	Cross-sectional	Convenience	56 105	W	Laboratory	Women undergoing pap smear 2006–14	Endocervical	Unclear	0·04%
Al-Sweih et al (2011)[99]	Kuwait	Cross-sectional	Convenience	5938	W	Primary health-care centre	Kuwaiti women	Vaginal	NAAT	1·9%
Al-Sweih et al (2011)[99]	Kuwait	Cross-sectional	Convenience	2601	W	Primary health-care centre	Expatriate women	Vaginal	NAAT	2·3%
Al-Sweih et al (2012)[100]	Kuwait	Case-control	Convenience	188	M	Gynaecology clinic	Fertile men	Semen	NAAT	3·7%
Deeb et al (2003)[101]	Lebanon	Cross-sectional	Multistage random sampling	506	W	Community	Ever-married women	Endocervical	ELISA	0
Hancali et al (2015)[102]	Morocco	Cross-sectional	Convenience	760	W	Family planning clinic	Family planning clinic attendees in 1999	Unclear	NAAT	4·0%
Hancali et al (2015)[102]	Morocco	Cross-sectional	Convenience	256	W	Family planning clinic	Family planning clinic attendees in 2011	Unclear	NAAT	4·4%

(Table 1 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Hulstein et al (2018)[103]	Morocco	Cross-sectional	Simple random sampling	163	M	Community	General population men	Serum	IFAT (IgG)	31·3%
Hulstein et al (2018)[103]	Morocco	Cross-sectional	Simple random sampling	174	W	Community	General population women	Serum	IFAT (IgG)	37·9%
Morocco Ministry of Health (2001)[104]	Morocco	Cross-sectional	Convenience	323	W	Antenatal clinic	Pregnant women	Urine	NAAT	2·7%
Morocco Ministry of Health (2001)[104]	Morocco	Cross-sectional	Convenience	518	W	Family planning clinic	Family planning clinic attendees	Urine	NAAT	5·2%
The Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project (2017)[105]	Morocco	Cross-sectional	Convenience	252	W	Antenatal clinic	Pregnant women	Unclear	NAAT	3·6%
The Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project (2017)[105]	Morocco	Cross-sectional	Convenience	537	W	Family planning clinic	Family planning clinic attendees	Unclear	NAAT	3%
Radouani et al (1998)[106]	Morocco	Case-control	Convenience	81	W	Hospital	Pregnant women	Serum	MIF (unclear)	14·8%
Radouani et al (1998)[106]	Morocco	Case-control	Convenience	200	M	Hospital	Blood donors	Serum	MIF (unclear)	4·5%
Takourt et al (1995)[107]	Morocco	Case-control	Convenience	200	M	Hospital	Blood donors	Serum	MIF (unclear)	5·0%
Takourt et al (1995)[107]	Morocco	Case-control	Convenience	200	W	Hospital	Blood donors	Serum	MIF (unclear)	10·0%
Mir et al (2009)[108]	Pakistan	Cross-sectional	Multistage systematic random sampling	2383	M	Community	General population men	Urine	NAAT	0
Wasti et al (1997)[109]	Pakistan	Cross-sectional	Convenience	300	W	Antenatal clinic and family planning clinic	Antenatal clinic and family planning clinic attendees	Endocervical	DFA	5·3%
Al-Thani et al (2013)[110]	Qatar	Cross-sectional	Convenience	133	W	Primary health-care centre	Qatari women	Endocervical	NAAT	5·3%
Al-Thani et al (2013)[110]	Qatar	Cross-sectional	Convenience	218	W	Primary health-care centre	Non-Qatari women	Endocervical	NAAT	5·5%
Alzahrani et al (2010)[111]	Saudi Arabia	Cross-sectional	Simple random sampling	95	W	Antenatal clinic	Pregnant women	Endocervical	ELISA	10·5%
Awad et al (2013)[112]	Saudi Arabia	Cross-sectional	Convenience	144	W	Gynaecology clinic	Antenatal clinic attendees	Urine	NAAT	11·1%
Bashi (1987)[113]	Saudi Arabia	Cross-sectional	Convenience	100	W	Primary health-care centre	Primary health-care centre attendees	Serum	MIF (IgG)	0
Bashi (1987)[113]	Saudi Arabia	Cross-sectional	Convenience	100	M	Primary health-care centre	Primary health-care centre attendees	Serum	MIF (IgG)	2%
Ghazi et al (2006)[114]	Saudi Arabia	Cross-sectional	Simple random sampling	1600	W	Antenatal clinic	Saudi pregnant women	Serum	ELISA (IgG)	8·7%
Ghazi et al (2006)[114]	Saudi Arabia	Cross-sectional	Simple random sampling	1460	W	Antenatal clinic	Saudi pregnant women	Serum	ELISA (IgM)	1·5%
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	112	M	Hospital	Blood donors	Serum	MIF (IgM)	0
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	112	M	Hospital	Blood donors	Serum	MIF (IgG)	1·8%
Kamel (2013)[116]	Saudi Arabia	Randomised controlled trial‡	Convenience	100	W	Antenatal clinic	Antenatal clinic attendees	Serum	ELISA (IgG)	4·0%
Massoud et al (1991)[117]	Saudi Arabia	Case-control	Convenience	100	W	Hospital	Asymptomatic women	Serum	IFAT (unclear)	0
Massoud et al (1991)[117]	Saudi Arabia	Case-control	Convenience	100	M	Hospital	Asymptomatic men	Serum	IFAT (unclear)	2·0%
Ismail et al (1990)[118]	Somalia	Cross-sectional	Convenience	194	W	Community	Women	Endocervical	EIA	12·4%

(Table 1 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Ismail et al (1990)[118]	Somalia	Cross-sectional	Convenience	189	M	Community	Men	Urethral	EIA	6%
Nur et al (2000)[119]	Somalia	Cross-sectional	Convenience	54	M	Hospital	Blood donors	Serum	EIA (IgG)	22·2%
WHO (2005a)[120]	Somalia	Cross-sectional	Convenience	4723	W	Antenatal clinic	Pregnant women	Urine	NAAT	1·7%
WHO (2005b)[121]	Somalia	Cross-sectional	Convenience	509	W	Antenatal clinic	Pregnant women	Urine	NAAT	1·4%
Ahmed et al (2018)[122]	Sudan	Case-control	Convenience	93	W	Hospital	Healthy pregnant women	Serum	ELISA (IgG)	0
Ahmed et al (2018)[122]	Sudan	Case-control	Convenience	93	W	Hospital	Pregnant women with pre-eclampsia	Serum	ELISA (IgG)	0
Almroth et al (2005)[123]	Sudan	Case-control	Convenience	139	W	Antenatal clinic	Antenatal clinic attendees	Serum	EIA (IgG)	3·6%
Ortashi et al (2004)[124]	Sudan	Cross-sectional	Convenience	151	W	Antenatal clinic	Pregnant women	Endocervical and urethral	EIA	19·9%
Alkayer et al (2017)[125]	Syria	Case-control	Convenience	21	W	Hospital	Pregnant women	Serum	ELISA (IgG)	4·7%
Ghazal-Aswad et al (2006)[126]	United Arab Emirates	Cross-sectional	Multistage cluster sampling	727	W	Clinics	Primary health-care centre and clinic attendees	Endocervical	EIA	2·5%

DFA=direct fluorescent assay. EIA=enzyme immunoassay. ELFA=enzyme-linked fluorescence assay. IFAT=indirect fluorescent antibody test. M=men or sample predominantly of men. MIF=micro-immunofluorescence. NAAT=nucleic acid amplification test. STI=sexually transmitted infection. W=women or sample predominantly of women. *Non-probability sampling refers to a sampling method in which the data collection process does not allow individuals to have equal chance of being selected; an example is convenience sampling for which individuals are selected on the basis of ease of accessibility (first-come first-served basis).[127,128] Probability-based sampling refers to a sampling method in which data collection process is based on a random selection of study participants; an example is random sampling from a sampling frame.[128] Another example of probability-based sampling is respondent-driven sampling, which is a sampling method specifically designed to sample hard-to-reach populations and is based on chain referral with the probability of selection calculated at each step in the network to produce adjusted prevalence estimates.[129] †The decimal places of the prevalence measures are as reported in the original report, but prevalence figures with more than one decimal place were rounded to one decimal place. ‡The extracted prevalence measure is for the baseline measurement.

Table 1: **Studies reporting *Chlamydia trachomatis* prevalence in general populations in the Middle East and north Africa**

by the median difference between year of publication and year of data collection (for studies with complete information). We did meta-regression diagnostics.

Factors associated with prevalence at p≤0·20 in univariable analysis were eligible for inclusion in the multivariable analysis. In the multivariable model, a p≤0·05 for any given factor indicated strong evidence for an association with *C trachomatis* prevalence. We did meta-regression models using Stata/SE (version 14).[34]

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the article. The corresponding author had full access to all the data in the study and had the final responsibility for the decision to submit for publication.

Results

The search identified a total of 1531 citations: 509 through PubMed, 557 through Embase, and 465 through regional and national databases. Of these citations, 302 reports underwent full-text screening after excluding duplicates and screening titles and abstracts. During full-text screening, 228 eligible reports were identified, and 74 were excluded for reasons outlined in figure 1. Hand-searching of reference lists of relevant reports and reviews yielded 14 additional eligible reports. 16 country-level reports were further identified through the Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project database. Three reports were subsequently excluded. In total, 255 reports contributing 552 prevalence measures or studies met the eligibility criteria for inclusion, but no incidence measures were identified.

Evidence covered 20 (87%) of 23 countries, encompassing a total of 256769 *C trachomatis* test results (tables 1 and 2; appendix pp 9–14). Iran contributed the largest number of measures or studies (n=176), followed by Egypt (n=89), Iraq (n=72), Saudi Arabia (n=45), Pakistan (n=42), and Morocco (n=32). Most studies assessed current infection (n=318), whereas the rest reported different serological measures (n=211), such as ever infection (anti-*C trachomatis* IgG; n=117). Details of *C trachomatis* testing protocol were specified in 424 (77%) of 552 studies; 320 (75%) of the 424 used commercial assays, 62 (15%) used in-house validated tests, 29 (7%) used culture, and 13 (3%) used a non-validated in-house test.

In general populations (n=137), prevalence of current genital infection ranged from 0 to 19·9% with a median of 3·0%, whereas ever infection prevalence ranged from 0 to 37·9% with a median of 4·7% (tables 1 and 3).

In populations at high risk (n=40), current infection prevalence in female sex workers (n=20) ranged from 0·9% to 72·9% with a median of 8·4%, whereas ever infection prevalence ranged from 19·8% to 100% with a median of 90·0% (tables 2 and 3). In men who have sex with men (including male sex workers and male-to-female transgenders; n=20), current infection prevalence ranged from 0 to 8·8% with a median of 1·2% for genital infections and from 3·6% to 18·3% with a median of 6·3% for rectal infections, but no ever infection measure was identified.

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
Populations at high risk										
Kadi et al (1990)[35]	Algeria	Cross-sectional	Convenience	44	W	Community	Female sex workers	Serum	MIF (IgG)	100%
El-Sayed et al (2002)[42]	Egypt	Cross-sectional	Convenience	52	W	Community	Female sex workers	Urine	NAAT	7·7%
El-Sayed et al (2002)[42]	Egypt	Cross-sectional	Convenience	80	M	Community	Men who have sex with men	Urine	NAAT	8·8%
Darougar et al (1983)[130]	Iran	Cross-sectional	Convenience	116	W	Community	Female sex workers	Endocervical	Culture	6·9%
Darougar et al (1983)[130]	Iran	Cross-sectional	Convenience	154	W	Community	Female sex workers	Serum	MIF (IgM)	29·2%
Darougar et al (1983)[130]	Iran	Cross-sectional	Convenience	154	W	Community	Female sex workers	Serum	MIF (IgG)	94·2%
Kassaian et al (2012)[131]	Iran	Cross-sectional	Convenience	91	W	Mixed	Female sex workers	Serum	ELISA (IgG)	19·8%
Kazerooni et al (2014)[132]	Iran	Cross-sectional	Respondent-driven sampling	278	W	Community	Female sex workers	Vaginal	NAAT	9%
Mirzazadeh et al (2016)[133]	Iran	Cross-sectional	Convenience	1337	W	Community	Female sex workers	Vaginal	NAAT	6%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	30	W	STI clinic	Women with multiple partners	Endocervical	ELFA	30%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	30	W	STI clinic	Women with multiple partners	Serum	IFAT (unclear)	36·7%
Bellaji et al (2017)[134]	Morocco	Cross-sectional	Convenience	519	W	NGOs	Female sex workers	Endocervical and vaginal	NAAT	20·7%
Morocco Ministry of Health (2008)[135]	Morocco	Cross-sectional	Convenience	141	W	STI clinic	Female sex workers	Endocervical and urine	NAAT	22·7%
Morocco Ministry of Health (2011)[136]	Morocco	Cross-sectional	Respondent-driven sampling	368	W	Community	Female sex workers in Agadir	Endocervical	NAAT	22·4%
Morocco Ministry of Health (2015)[137]	Morocco	Cross-sectional	Respondent-driven sampling	247	M	Community	Men who have sex with men in Agadir	Urine	NAAT	5·4%
Morocco Ministry of Health (2015)[137]	Morocco	Cross-sectional	Respondent-driven sampling	252	M	Community	Men who have sex with men in Marrakech	Urine	NAAT	6·5%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	426	W	Community	Female sex workers in Rawalpindi	Endocervical	NAAT	1·7%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	107	W	Community	Female sex workers in Abbottabad	Endocervical	NAAT	0·9%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	195	M	Community	Male sex workers in Rawalpindi (Bantha)	Urine	NAAT	0
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	195	M	Community	Male sex workers in Rawalpindi (Bantha)	Rectal	NAAT	4·7%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	364	M	Community	Male sex workers in Rawalpindi (Khotki)	Urine	NAAT	0
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	364	M	Community	Male sex workers in Rawalpindi (Khotki)	Rectal	NAAT	3·6%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	253	M	Community	Male sex workers in Rawalpindi (Khusra)	Urine	NAAT	0
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	253	M	Community	Male sex workers in Rawalpindi (Khusra)	Rectal	NAAT	9·9%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	83	M	Community	Male sex workers in Abbottabad (Bantha)	Urine	NAAT	1·2%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	83	M	Community	Male sex workers in Abbottabad (Bantha)	Rectal	NAAT	4·9%
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	20	M	Community	Male sex workers in Abbottabad (Khotki and Khusra)	Urine	NAAT	0
Hawkes et al (2009)[138]	Pakistan	Cross-sectional	Respondent-driven sampling	20	M	Community	Male sex workers in Abbottabad (Khotki and Khusra)	Rectal	NAAT	6·3%
Khan et al (2011)[139]	Pakistan	Cross-sectional	Respondent-driven sampling	730	W	Community	Female sex workers in Lahore	Endocervical	NAAT	7·7%
Osama (2017)[140]	Pakistan	Cross-sectional	Convenience	2531	M	Drop in centre	Men who have sex with men in Lahore	Unclear	Unclear	35·2%
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Systematic random sampling	383	W	Red-light	Female sex workers in Lahore	Endocervical	NAAT	11%
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Snowball	348	W	Community	Female sex workers in Karachi	Endocervical	NAAT	5·2%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Respondent-driven sampling	395	M	Community	Male sex workers in Lahore	Urethral	NAAT	1·5%
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Snowball	396	M	Community	Male sex workers in Karachi	Urethral	NAAT	1·2%
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Snowball	394	M	Community	Male sex workers in Karachi	Rectal	NAAT	10·4%
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Systematic random cluster sampling	198	M	Community	Hijras in Lahore	Urethral	NAAT	1·5%
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Systematic random cluster sampling	197	M	Community	Hijras in Karachi	Urethral	NAAT	0
Rehan et al (2009)[141]	Pakistan	Cross-sectional	Systematic random cluster sampling	197	M	Community	Hijras in Karachi	Rectal	NAAT	18·3%
Znazen et al (2010)[142]	Tunisia	Cross-sectional	Convenience	188	W	Community	Female sex workers	Endocervical	NAAT	72·9%
Znazen et al (2010)[142]	Tunisia	Cross-sectional	Convenience	183	W	Community	Female sex workers	Serum	MIF (IgG)	85·8%
Infertility clinic attendees										
Abdel Aleem et al (1996)[143]	Egypt	Case-control	Convenience	144	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	52%
Abdel Aleem et al (1996)[143]	Egypt	Case-control	Convenience	104	M	Infertility clinic	Men with unclear infertility diagnosis	Serum	ELISA (IgG)	24%
Abdel Monem et al (2005)[36]	Egypt	Case-control	Convenience	150	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	Culture	24%
Abdel Monem et al (2005)[36]	Egypt	Case-control	Convenience	150	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	EIA	22·7%
Abdella et al (2015)[144]	Egypt	Case-control	Convenience	50	W	Infertility clinic	Women with idiopathic infertility	Serum	ELISA (IgM)	4%
Abdella et al (2015)[144]	Egypt	Case-control	Convenience	50	W	Infertility clinic	Women with idiopathic infertility	Serum	ELISA (IgG)	36%
Abdella et al (2015)[144]	Egypt	Case-control	Convenience	50	W	Infertility clinic	Women with idiopathic infertility	Endocervical	NAAT	6%
Azab and Hassouna (2008)[145]	Egypt	Cross-sectional	Convenience	70	W	Infertility clinic	Nearly half of women with TFI	Serum	ELISA (IgG)	28·6%
Badary (1996)[38]	Egypt	Case-control	Convenience	60	W	Infertility clinic	Women with idiopathic infertility	Endocervical	DFA	33%
Berry and El Shabrawy (1996)[39]	Egypt	Case-control	Convenience	70	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	EIA (IgG)	18·6%
Elkayal et al (2015)[146]	Egypt	Case-control	Convenience	100	W	Infertility clinic	Women with mixed infertility diagnosis	Endocervical	ELISA	3%
Elkayal et al (2015)[146]	Egypt	Case-control	Convenience	100	W	Infertility clinic	Women with mixed infertility diagnosis	Endocervical	NAAT	3%
El Sayed et al (1997)[147]	Egypt	Cross-sectional	Convenience	22	W	Infertility clinic	Women with TFI	Serum	MIF (IgG)	81·8%
El Sayed et al (1997)[147]	Egypt	Cross-sectional	Convenience	78	W	Infertility clinic	Women without TFI	Serum	MIF (IgG)	7·7%
Inhorn and Buss (1993)[148]	Egypt	Case-control	Convenience	83	W	Hospital	Majority of women without TFI	Unclear	Unclear	33%
Makled et al (2013)[149]	Egypt	Cross-sectional	Simple random sampling	27	W	Infertility clinic	Women with TFI	Serum	ELISA (IgG)	85·2%
Makled et al (2013)[149]	Egypt	Cross-sectional	Simple random sampling	51	W	Infertility clinic	Women without TFI	Serum	ELISA (IgG)	13·7%
Nada et al (2015)[45]	Egypt	Case-control	Convenience	100	W	Infertility clinic	Women with idiopathic infertility	Endocervical	NAAT	15%
Sadek et al (1993)[150]	Egypt	Case-control	Convenience	43	W	Infertility clinic	Infertile women in infertile couples with sperm antibodies	Unclear	DFA	18·6%
Sadek et al (1993)[150]	Egypt	Case-control	Convenience	37	W	Infertility clinic	Women partners in infertile couples with sperm antibodies	Unclear	DFA	18·9%
Sadek et al (1993)[150]	Egypt	Case-control	Convenience	62	M	Infertility clinic	Men partners in infertile couples with sperm antibodies	Unclear	DFA	19·4%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Sadek et al (1993)[150]	Egypt	Case-control	Convenience	18	M	Infertility clinic	Infertile men in infertile couples with sperm antibodies	Unclear	DFA	22·2%
Siam and Hefzy (2012)[151]	Egypt	Case-control	Convenience	90	W	Gynaecology clinic	Women with idiopathic infertility	Serum	ELISA (IgG)	20%
Siam and Hefzy (2012)[151]	Egypt	Case-control	Convenience	90	W	Gynaecology clinic	Women with idiopathic infertility	Urine	NAAT	4·4%
Younis et al (2000)[152]	Egypt	Cross-sectional	Convenience	30	W	Infertility clinic	Women with TFI	Serum	MIF (IgG)	46·7%
Younis et al (2000)[152]	Egypt	Cross-sectional	Convenience	14	W	Infertility clinic	Women without TFI	Serum	MIF (IgG)	50·0%
Zaitun and Zaitoun (1990)[153]	Egypt	Cross-sectional	Convenience	20	W	Infertility clinic	Women with TFI	Serum	Unclear	25%
Zaitun and Zaitoun (1990)[153]	Egypt	Cross-sectional	Convenience	30	W	Infertility clinic	Women without TFI	Serum	Unclear	3·3%
Zaki (1989)[47]	Egypt	Cross-sectional	Convenience	100	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	Culture	7%
Zytoon (1994)[154]	Egypt	Cross-sectional	Convenience	75	W	Infertility clinic	Women with mixed infertility diagnosis	Endocervical	Culture	65·3%
Ahmadi et al (2018)[49]	Iran	Case-control	Convenience	165	M	Infertility clinic	Men with male factor infertility	Semen	NAAT	4·2%
Badami and Salari (2001)[51]	Iran	Case-control	Convenience	125	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	DFA	8·8%
Badami and Salari (2001)[51]	Iran	Case-control	Convenience	125	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	Unclear	20·8%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Infertility clinic	Women with mixed infertility diagnosis	Urine	NAAT	4·8%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	M	Infertility clinic	40% of men had male factor infertility	Urine	NAAT	4·4%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	EIA (IgM)	4%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgA)	0
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	15·6%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	M	Infertility clinic	40% of men had male factor infertility	Serum	EIA (IgM)	1·2%
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	M	Infertility clinic	40% of men had male factor infertility	Serum	ELISA (IgA)	0
Dehghan et al (2017)[57]	Iran	Case-control	Convenience	250	M	Infertility clinic	40% of men had male factor infertility	Serum	ELISA (IgG)	18%
Golshani et al (2007)[155]	Iran	Cross-sectional	Convenience	200	M	Infertility clinic	Majority of men had male factor infertility	Semen	NAAT	18·0%
Goshayeshi et al (2015)[58]	Iran	Case-control	Convenience	100	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	NAAT	21·0%
Hajikhani et al (2013)[156]	Iran	Cross-sectional	Convenience	51	W	Infertility clinic	Women with TFI	Endocervical	Culture	3·9%
Hajikhani et al (2013)[156]	Iran	Cross-sectional	Convenience	51	W	Infertility clinic	Women with TFI	Endocervical	NAAT	11·7%
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	32	W	Infertility clinic	Women with TFI	Vaginal	NAAT	9·4%
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	68	W	Infertility clinic	Women with ovarian and other infertility	Vaginal	NAAT	2·9%
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	32	W	Infertility clinic	Women with TFI	Serum	ELISA (IgM)	9·4%
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	68	W	Infertility clinic	Women with ovarian and other infertility	Serum	ELISA (IgM)	4·4%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	32	W	Infertility clinic	Women with TFI	Serum	ELISA (IgG)	0
Joolayi et al (2017)[62]	Iran	Case-control	Convenience	68	W	Infertility clinic	Women with ovarian and other infertility	Serum	ELISA (IgG)	0
Kajbaf and Gholamnezhad (1998)[63]	Iran	Case-control	Convenience	101	W	Infertility clinic	Women with mixed infertility diagnosis	Endocervical	DFA	7·9%
Kajbaf and Gholamnezhad (1998)[63]	Iran	Case-control	Convenience	101	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	17·8%
Kalantar et al (2007)[157]	Iran	Cross-sectional	Convenience	91	W	Infertility clinic	Majority of women had female factor infertility	Serum	ELISA (IgG)	0
Kalantar et al (2007)[157]	Iran	Cross-sectional	Convenience	91	W	Infertility clinic	Majority of women had female factor infertility	Vaginal	NAAT	0
Kamyabi (2009)[64]	Iran	Case-control	Convenience	35	W	Gynaecology clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	22·9%
Mansour Ghanaie (2014)[158]	Iran	Cross-sectional	Convenience	135	W	Infertility clinic	Majority of women without TFI	Endocervical	NAAT	19·3%
Ministry of Health and Medical Education (2008)[67]	Iran	Case-control	Convenience	46	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	ELISA (IgG)	23·9%
Marashi et al (2014)[66]	Iran	Case-control	Convenience	150	W	Infertility clinic	Women with idiopathic infertility	Endocervical	DFA	15·3%
Marashi et al (2014)[66]	Iran	Case-control	Convenience	150	W	Infertility clinic	Women with idiopathic infertility	Endocervical	NAAT	32%
Ministry of Health and Medical Education (2008)[67]	Iran	Case-control	Convenience	125	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	DFA	8·8%
Ministry of Health and Medical Education (2008)[67]	Iran	Cross-sectional	Convenience	100	M	Infertility clinic	Men with unclear infertility diagnosis	Unclear	NAAT	9%
Moazenchi et al (2018)[159]	Iran	Cross-sectional	Convenience	1080	M	Infertility clinic	Men with unclear infertility diagnosis	Serum	ELISA (IgA)	4·3%
Moazenchi et al (2018)[159]	Iran	Cross-sectional	Convenience	1080	M	Infertility clinic	Men with unclear infertility diagnosis	Semen	NAAT	10%
Mousavi et al (2014)[69]	Iran	Case-control	Convenience	104	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	NAAT	4·8%
Nan Bakhsh et al (2008)[160]	Iran	Cross-sectional	Convenience	144	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	11·1%
Nikbakht et al (2008)[161]	Iran	Case-control	Convenience	125	W	Infertility clinic	Women with TFI	Unclear	ELISA (unclear)	23·2%
Peivandi et al (2009)[162]	Iran	Cross-sectional	Convenience	110	W	Infertility clinic	Majority of women with TFI	Serum	MIF (IgG)	24·5%
Rashidi et al (2007)[163]	Iran	Cross-sectional	Convenience	300	W	Infertility clinic	Women with mixed infertility diagnosis	Unclear	ELISA (unclear)	32·3%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	44	W	Infertility clinic	Women with TFI	Urine	NAAT	4·5%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	190	W	Infertility clinic	Women with ovarian and other infertility	Urine	NAAT	14·2%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	44	W	Infertility clinic	Women with TFI	Serum	ELISA (IgM)	2·3%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	190	W	Infertility clinic	Women with ovarian and other infertility	Serum	ELISA (IgM)	0·5%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	44	W	Infertility clinic	Women with TFI	Serum	ELISA (IgG)	9·1%
Rashidi et al (2013)[71]	Iran	Case-control	Convenience	190	W	Infertility clinic	Women with ovarian and other infertility	Serum	ELISA (IgG)	8·4%
Sadrpour et al (2013)[164]	Iran	Cross-sectional	Convenience	120	M	Infertility clinic	Men with male factor infertility	Semen	NAAT	3%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Sattari et al (2017)[75]	Iran	Case-control	Convenience	184	W	Infertility clinic	Majority of women without TFI	Serum	ELISA (IgM)	5·4%
Sattari et al (2017)[75]	Iran	Case-control	Convenience	184	W	Infertility clinic	Majority of women without TFI	Serum	ELISA (IgG)	35·9%
Siahkali and Amini (2018)[165]	Iran	Cross-sectional	Convenience	60	M	Infertility clinic	Men with idiopathic infertility	Semen	NAAT	5·0%
Abid and Al-Zwaid (2015)[166]	Iraq	Case-control	Convenience	61	W	Infertility clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	30%
Ahmed (2012)[167]	Iraq	Case-control	Convenience	47	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	NAAT	29·8%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	54	W	Infertility clinic	Women with unclear infertility diagnosis	Endocervical	ELFA	9·3%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	54	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	IFAT (unclear)	11·1%
Ali and Al-Kazaz (2018)[85]	Iraq	Case-control	Convenience	63	M	Clinic	Men with male factor infertility	Semen	NAAT	17·4%
Al-Kattan and Mohammed (2013)[168]	Iraq	Cross-sectional	Convenience	54	W	Infertility clinic	Women with TFI or adhesions	Serum	ELISA (IgG)	51·9%
Al-Kattan and Mohammed (2013)[168]	Iraq	Cross-sectional	Convenience	67	W	Infertility clinic	Women without TFI or endometriosis	Serum	ELISA (IgG)	29·9%
Dawood (2011)[169]	Iraq	Cross-sectional	Convenience	30	W	Hospital	Women with unclear infertility diagnosis	Serum	ELISA (IgM)	86·6%
Dawood (2011)[169]	Iraq	Cross-sectional	Convenience	30	W	Hospital	Women with unclear infertility diagnosis	Serum	ELISA (IgA)	3·3%
Dawood (2011)[169]	Iraq	Cross-sectional	Convenience	30	W	Hospital	Women with unclear infertility diagnosis	Serum	ELISA (IgG)	53·3%
Dawood (2011)[169]	Iraq	Cross-sectional	Convenience	100	W	Hospital	Women with unclear infertility diagnosis	Endocervical	NAAT	30%
Ismail and Ali (2012)[88]	Iraq	Case-control	Convenience	52	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	ELISA (IgG)	25%
Ismail and Ali (2012)[88]	Iraq	Case-control	Convenience	52	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	ELISA (IgM)	42·3%
Ismail and Ali (2012)[88]	Iraq	Case-control	Convenience	52	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	ELISA (IgA)	3·8%
Mohammed et al (2017)[90]	Iraq	Case-control	Convenience	80	W	Gynaecology clinic	Women with mixed infertility diagnosis	Endocervical	NAAT	13·8%
Mohammed et al (2017)[90]	Iraq	Case-control	Convenience	80	W	Gynaecology clinic	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	2·5%
Yahya and Al-Siraj (2009)[91]	Iraq	Cross-sectional	Convenience	296	M	Laboratory	Men with unclear infertility diagnosis	Serum	Culture	4·0%
Abusarah et al (2013)[92]	Jordan	Case-control	Convenience	81	M	Gynaecology clinic	Men with male factor infertility	Urine	NAAT	4·9%
Al-Ramahi et al (2008)[93]	Jordan	Case-control	Convenience	66	W	Infertility clinic	Women with idiopathic infertility	Endocervical	NAAT	3·0%
Al-Ramahi et al (2008)[93]	Jordan	Case-control	Convenience	19	W	Infertility clinic	Women with TFI	Endocervical	NAAT	0
Al-Ramahi et al (2008)[93]	Jordan	Case-control	Convenience	38	W	Infertility clinic	Women with male factor infertility	Endocervical	NAAT	7·9%
Al-Ramahi et al (2008)[93]	Jordan	Case-control	Convenience	29	W	Infertility clinic	Women with ovarian infertility	Endocervical	NAAT	3·4%
Al-Sweih et al (2012)[100]	Kuwait	Case-control	Convenience	127	M	Infertility clinic	Men with unclear infertility diagnosis	Semen	NAAT	3·9%
Radouani et al (1998)[106]	Morocco	Case-control	Convenience	200	M	Infertility clinic	Majority of men had male factor infertility	Serum	MIF (unclear)	21·5%
Radouani et al (1998)[106]	Morocco	Case-control	Convenience	81	W	Infertility clinic	Women with unclear infertility diagnosis	Serum	MIF (unclear)	44·4%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Al Subhi et al (2013)[170]	Oman	Cross-sectional	Convenience	51	W	Infertility clinic	Women with TFI	Endocervical	EIA	5·9%
Al Subhi et al (2013)[170]	Oman	Cross-sectional	Convenience	167	W	Infertility clinic	Women without TFI	Endocervical	EIA	4·8%
Qayum and Khalid-bin-Saleem (2013)[171]	Pakistan	Cross-sectional	Convenience	80	W	Gynaecology clinic	Women with unclear infertility diagnosis	Urine	Unclear	7·5%
Al-Hindi et al (2010)[172]	Palestine	Cross-sectional	Convenience	69	W	Infertility clinic	Women undergoing IVF in 2000	Serum	ELISA (IgM)	11·6%
Al-Hindi et al (2010)[172]	Palestine	Cross-sectional	Convenience	268	W	Infertility clinic	Women undergoing IVF in 2001	Serum	ELISA (IgM)	23·9%
Al-Hindi et al (2010)[172]	Palestine	Cross-sectional	Convenience	316	W	Infertility clinic	Women undergoing IVF in 2002	Serum	ELISA (IgM)	33·5%
Al-Hindi et al (2010)[172]	Palestine	Cross-sectional	Convenience	399	W	Infertility clinic	Women undergoing IVF in 2003	Serum	ELISA (IgM)	9·3%
Al-Hindi et al (2010)[172]	Palestine	Cross-sectional	Convenience	586	W	Infertility clinic	Women undergoing IVF in 2004	Serum	ELISA (IgM)	4·6%
Al-Hindi et al (2010)[172]	Palestine	Cross-sectional	Convenience	316	W	Infertility clinic	Women undergoing IVF in 2005	Serum	ELISA (IgM)	2·8%
Abdul Jabbar (1990)[173]	Saudi Arabia	Cross-sectional	Convenience	13	W	Infertility clinic	Women with TFI	Endocervical	DFA	53·8%
Abdul Jabbar (1990)[173]	Saudi Arabia	Cross-sectional	Convenience	18	W	Infertility clinic	Women without TFI	Endocervical	DFA	11·1%
Abdul Jabbar (1990)[173]	Saudi Arabia	Cross-sectional	Convenience	34	M	Infertility clinic	Men with unclear infertility diagnosis	Urethral	DFA	26·4%
Alfarraj et al (2015)[174]	Saudi Arabia	Case-control	Convenience	100	W	Infertility clinic	Women with mixed infertility diagnosis	Endocervical	NAAT	8·0%
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	41	W	Gynaecology clinic	Women with unclear infertility diagnosis	Endocervical	Culture	9·5%
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	41	W	Gynaecology clinic	Women with unclear infertility diagnosis	Serum	MIF (IgM)	0
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	41	W	Gynaecology clinic	Women with unclear infertility diagnosis	Serum	MIF (IgG)	16·7%
Kamel (2013)[116]	Saudi Arabia	Randomised controlled trial‡	Convenience	640	W	Gynaecology clinic	Women with unclear infertility diagnosis	Endocervical	Culture	12·0%
Kamel (2013)[116]	Saudi Arabia	Randomised controlled trial‡	Convenience	640	W	Gynaecology clinic	Women with unclear infertility diagnosis	Serum	ELISA (IgA)	5%
Kamel (2013)[116]	Saudi Arabia	Randomised controlled trial‡	Convenience	640	W	Gynaecology clinic	Women with unclear infertility diagnosis	Serum	ELISA (IgG)	8·0%
Sabra and Al-Harbi (2014)[175]	Saudi Arabia	Cross-sectional	Convenience	148	M	Infertility clinic	Men with male factor infertility	Semen	Giemsa stain	8·1%
Almroth et al (2005)[123]	Sudan	Case-control	Convenience	81	W	Infertility clinic	More than half of women with TFI	Serum	EIA (IgG)	14%
Alkayer et al (2017)[125]	Syria	Case-control	Convenience	23	W	Hospital	Women with mixed infertility diagnosis	Serum	ELISA (IgG)	17·1%
Gdoura et al (2001a)[176]	Tunisia	Cross-sectional	Convenience	92	M	Infertility clinic	Men with unclear infertility diagnosis	Urethral	NAAT	18·5%
Gdoura et al (2001b)[177]	Tunisia	Cross-sectional	Convenience	92	M	Infertility clinic	Men with unclear infertility diagnosis	Serum	MIF (IgG)	9·8%
Gdoura et al (2001a)[176]	Tunisia	Cross-sectional	Convenience	92	M	Infertility clinic	Men with unclear infertility diagnosis	Urethral	DFA	4·3%
Gdoura et al (2001a)[176]	Tunisia	Cross-sectional	Convenience	92	M	Infertility clinic	Men with unclear infertility diagnosis	Urethral	Culture	1·1%
Gdoura et al (2001a)[176]	Tunisia	Cross-sectional	Convenience	92	M	Infertility clinic	Men with unclear infertility diagnosis	Urethral	Unclear	8·7%
Gdoura et al (2001b)[177]	Tunisia	Cross-sectional	Convenience	92	W	Infertility clinic	Partners of infertile men	Endocervical	NAAT	26·1%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Gdoura et al (2001b)[177]	Tunisia	Cross-sectional	Convenience	92	W	Infertility clinic	Partners of infertile men	Serum	MIF (IgG)	17·4%
Gdoura et al (2008)[178]	Tunisia	Cross-sectional	Convenience	104	M	Infertility clinic	Men with male factor infertility	Urine	NAAT	39·4%
Sellami et al (2014)[179]	Tunisia	Cross-sectional	Convenience	85	M	Infertility clinic	Men with unclear infertility diagnosis	Semen	NAAT	15·2%
Women with miscarriage (or abortion of unknown cause)										
Zaki (1989)[47]	Egypt	Cross-sectional	Convenience	100	W	Gynaecology clinic	Presenting with abortion	Endocervical	Culture	5%
Ahmadi et al (2016b)[180]	Iran	Case-control	Convenience	109	W	Family planning clinic	Spontaneous abortion	Endocervical	NAAT	22·9%
Bagheri and Roghanian (2014)[181]	Iran	Cross-sectional	Convenience	70	W	Hospital	Recent or recurrent miscarriage	Vaginal	NAAT	1·4%
Bagheri et al (2018)[53]	Iran	Case-control	Convenience	97	W	Fertility centre	Recent or recurrent miscarriage	Vaginal	NAAT	11·3%
Bagheri et al (2018)[53]	Iran	Case-control	Convenience	97	W	Fertility centre	Recent or recurrent miscarriage	Serum	ELISA (IgA)	2·1%
Bagheri et al (2018)[53]	Iran	Case-control	Convenience	97	W	Fertility centre	Recent or recurrent miscarriage	Serum	ELISA (IgG)	4·1%
Jahromi et al (2010)[60]	Iran	Case-control	Convenience	220	W	Gynaecology clinic	Spontaneous abortion	Endocervical	DFA	25·5%
Massiha et al (2010)[182]	Iran	Cross-sectional	Convenience	84	W	Hospital	Presenting with abortion	Unclear	Unclear	2·3%
Salari and Badami (2002)[183]	Iran	Case-control	Convenience	125	W	Hospital	Recurrent abortion	Endocervical	DFA	7·2%
Sisakht et al (2017)[76]	Iran	Case-control	Convenience	77	W	Gynaecology clinic	Spontaneous abortion	Urine	NAAT	9·3%
Zahirnia et al (2018)[78]	Iran	Cross-sectional	Convenience	124	W	Gynaecology clinic	Presenting with abortion	Vaginal	NAAT	15·3%
Abdul-Karim et al (2009)[80]	Iraq	Case-control	Convenience	79	W	Hospital	Presenting with abortion	Serum	ELISA (IgG)	6·4%
Abdulkhudher et al (2014)[79]	Iraq	Case-control	Convenience	60	W	Antenatal clinic	Recent or recurrent miscarriage	Serum	ELISA (IgM)	38·3%
Abdulkhudher et al (2014)[79]	Iraq	Case-control	Convenience	60	W	Antenatal clinic	Recent or recurrent miscarriage	Serum	ELISA (IgG)	33·3%
Ahmed (2008)[82]	Iraq	Case-control	Convenience	60	W	Hospital	Recurrent miscarriage	Serum	ELISA (unclear)	0
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	89	W	Family planning clinic	Recent or recurrent abortion	Endocervical	ELFA	12·4%
Al-Husseinei et al (2009)[84]	Iraq	Case-control	Convenience	89	W	Family planning clinic	Recent or recurrent abortion	Serum	IFAT (unclear)	14·6%
Alkhafaf (2013)[86]	Iraq	Case-control	Convenience	123	W	Hospital	Spontaneous abortion	Serum	ELISA (IgG)	17·1%
Al-Nuaimy and Al-Jandeel (2018)[184]	Iraq	Case-control	Convenience	120	W	Hospital	Recent or recurrent abortion	Endocervical	NAAT	17·5%
Al-Nuaimy and Al-Jandeel (2018)[184]	Iraq	Case-control	Convenience	120	W	Hospital	Recent or recurrent abortion	Serum	ELISA (IgG)	14·2%
Mohammed et al (2012)[89]	Iraq	Case-control	Convenience	62	W	Gynaecology clinic	Three or more miscarriages	Serum	ELISA (IgM)	16·1%
Mohammed et al (2012)[89]	Iraq	Case-control	Convenience	34	W	Gynaecology clinic	Less than three miscarriages	Serum	ELISA (IgM)	29·4%
Salman (2016)[185]	Iraq	Cross-sectional	Convenience	184	W	Gynaecology clinic	Presenting with abortion	Serum	ELISA (IgM)	21·2%
Salman (2016)[185]	Iraq	Cross-sectional	Convenience	184	W	Gynaecology clinic	Presenting with abortion	Serum	ELISA (IgG)	8·2%
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	12	W	Hospital	Recurrent miscarriage	Endocervical	Culture	16·7%

(Table 2 continues on next page)

	Country	Study design	Sampling*	Sample size	Sex	Study context	Population characteristics	Specimen	Assay type	Prevalence†
(Continued from previous page)										
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	12	W	Hospital	Recurrent miscarriage	Serum	MIF (IgM)	0
Hossain (1988)[115]	Saudi Arabia	Cross-sectional	Convenience	12	W	Hospital	Recurrent miscarriage	Serum	MIF (IgG)	16·7%
Women with ectopic pregnancy										
Diab (1993)[40]	Egypt	Case-control	Convenience	30	W	Family planning clinic	Ectopic pregnancy	Serum	EIA (IgG)	30%
Abdullah (2012)[81]	Iraq	Case-control	Convenience	24	W	Hospital	Ectopic pregnancy	Serum	ELISA (IgM)	4%
Abdullah (2012)[81]	Iraq	Case-control	Convenience	24	W	Hospital	Ectopic pregnancy	Serum	ELISA (IgG)	45%

DFA=direct fluorescent assay. EIA=enzyme immunoassay. ELFA=enzyme-linked fluorescence assay. IFAT=indirect fluorescent antibody test. M=men or sample predominantly of men. MIF=micro-immunofluorescence. NAAT=nucleic acid amplification test. NGOs=non-governmental organisations. STI=sexually transmitted infection. TFI=tubal factor infertility. W=women or sample predominantly of women. *Non-probability sampling refers to a sampling method in which the data collection process does not allow individuals to have equal chance of being selected; an example is convenience sampling for which individuals are selected on the basis of ease of accessibility (first-come first-served basis).[127,128] Probability-based sampling refers to a sampling method in which data collection process is based on a random selection of study participants; an example is random sampling from a sampling frame.[128] Another example of probability-based sampling is respondent-driven sampling, which is a sampling method specifically designed to sample hard-to-reach populations and is based on chain referral with the probability of selection calculated at each step in the network to produce adjusted prevalence estimates.[129] †The decimal places of the prevalence measures are as reported in the original report, but prevalence figures with more than one decimal place were rounded to one decimal place. ‡The extracted prevalence measure is for the baseline measurement.

Table 2: **Studies reporting *Chlamydia trachomatis* prevalence in populations at high risk, infertility clinic attendees, women with miscarriage, and women with ectopic pregnancy in the Middle East and north Africa**

High prevalence was observed in infertility clinic attendees, for both women and men (n=135), in which current infection prevalence ranged from 0 to 65·3% with a median of 9·2%, whereas ever infection prevalence ranged from 0 to 85·2% with a median of 18·6% (tables 2 and 3). Similarly, high prevalence was observed in women with miscarriage (n=27), in which current infection prevalence ranged from 1·4% to 25·5% with a median of 12·4%, whereas ever infection prevalence ranged from 4·1% to 33·3% with a median of 14·2% (tables 2 and 3).

Table 3 summarises the prevalence for other at-risk populations, and table 2 and the appendix (pp 9–14) include the full data.

The summarised and study-specific risk of bias and precision assessments are shown in the appendix (pp 15–27). Briefly, 166 (30·1%) of 552 prevalence measures were based on samples including 200 participants or more, and were classified as having higher precision. Although convenience sampling was the most common sampling methodology (495 [89·7%] of 552), probability-based sampling methods, such as respondent-driven sampling, are of increasing use for populations at high risk (18 [45%] of 40 studies in female sex workers and men who have sex with men). Almost all studies (524 [94·9%] of 552) specified the type of biological assay used for infection ascertainment (low risk of bias for this domain). Response rate was, however, unclear for 417 (75·5%) of 552 studies. Prevalence studies were overall of reasonable quality; only eight (1·4%) of 552 had high risk of bias in two or more quality domains.

Table 3 shows the meta-analyses' results for the pooled average *C trachomatis* prevalence for each at-risk population, stratified by type of assay used for infection ascertainment. Current infection prevalence was estimated at 3·0% (95% CI 2·3–3·8) in general populations, 2·8% (1·0–5·2) in populations at intermediate risk, 13·2% (7·2–20·7) in female sex workers, 1·2% (0·2–2·8) for genital infections and 7·7% (4·2–12·0) for rectal infections in men who have sex with men, 11·3% (9·0–13·7) in infertility clinic attendees, 12·4% (7·9–17·7) in women with miscarriage, 12·4% (9·4–15·7) in symptomatic women, and 17·4% (12·5–22·8) in symptomatic men.

Meanwhile, pooled average prevalence of ever infection was estimated at 6·9% (4·3–10·0) in general populations, 1·4% (0·8–2·4) in populations at intermediate risk, 80·9% (43·8–100) in female sex workers, 21·5% (16·3–27·2) in infertility clinic attendees, 12·4% (6·6–19·5) in women with miscarriage, 37·1% (22·4–53·0) in women with ectopic pregnancy, 22·7% (15·4–31·0) in symptomatic women, and 16·9% (9·4–25·8) in symptomatic men (table 3).

Evidence for heterogeneity in *C trachomatis* prevalence estimates was observed; p values for Cochran's *Q* statistic was <0·0001 in most meta-analyses (table 3). Prediction intervals were generally wide affirming high heterogeneity. I^2 was also mostly more than 70%, indicating that most variability is due to true differences in effect size across studies rather than chance.

Figures 2 and 3 and the appendix (pp 28–40) summarise the results of subgroup meta-analyses in various subpopulations. These data show the results stratified by sex or by genital versus rectal infection (the latter only for men who have sex with men), for studies reporting current infection prevalence based on NAAT and those reporting ever infection prevalence, as well as by assay type for studies reporting current infection prevalence. Subgroup meta-analyses in infertile populations stratified by infertility diagnosis and by assay type are shown in the appendix (pp 41–42).

Table 4 summarises results of the meta-regression analyses. In the univariable analyses, at-risk population, assay type, sampling methodology, sample size, year of publication, year of data collection, country, response rate, and sex were associated with prevalence at p≤0·2. Alignment with meta-regression underlying assumption

	Studies (n)	Samples		*C trachomatis* prevalence (median [range])	Pooled average *C trachomatis* prevalence (estimate [95% CI])	Heterogeneity measures		
		Tested	*C trachomatis* positive			Q (p value)*	I^2† (95% CI)	Prediction interval‡
General populations								
Current genital infection								
NAAT	48	25 397	748	2·9% (0–15·5)	3·1 (2·2–4·2)	714·3 (p<0·0001)	91·4% (89·4–93·0)	0·0–12·4
Culture	4	4464	55	5·8% (1·0–15·0)	4·3 (0·3–11·4)	22·5 (p<0·0001)	86·6% (67·7–94·5)	0·0–50·9
Other§	23	128 013	328	3·5% (0–19·9)	2·4 (1·6–3·4)	722·3 (p<0·0001)	97·0% (96·2–97·5)	0·0–7·2
Overall current genital infection	75	157 874	1131	3·0% (0–19·9)	3·0 (2·3–3·8)	2703·5 (p<0·0001)	97·3% (96·9–97·6)	0·0–10·9
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	35	5877	525	4·7% (0–37·9)	6·9 (4·3–10·0)	226·1 (p<0·0001)	86·7% (82·2–90·1)	0·0–30·2
IgM (recent infection)	13	2843	74	1·6% (0–14·0)	1·8 (0·3–3·9)	77·7 (p<0·0001)	84·6% (75·1–90·4)	0·0–12·4
IgA	4	377	12	4·3% (0–40·4)	6·2 (0·0–21·6)	37·8 (p<0·0001)	92·1% (82·9–96·3)	0·0–93·7
Not specified (IgG, IgM, or IgA)	9	1081	61	4·5% (0–14·8)	4·3 (1·9–7·4)	34·5 (p<0·0001)	76·8% (55·7–87·8)	0·0–17·3
Unclear	1	250	8	..	3·2 (1·4–6·2)	..	..	..
Populations at intermediate risk								
Current genital infection								
NAAT	12	2815	69	1·5% (0–38·0)	2·6 (0·8–5·2)	117·4 (p<0·0001)	75·6% (56·0–86·5)	0·0–16·1
Culture	..	..	..	..	..	..	..	..
Other§	1	308	15	..	4·9 (2·8–7·9	..	..	..
Overall current genital infection	13	3123	84	2·0% (0–38·0)	2·8 (1·0–5·2)	127·0 (p<0·0001)	90·6% (85·7–93·8)	0·0–15·8
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	1	1041	15	..	1·4 (0·8–2·4)	..	..	..
IgM (recent infection)	..	..	..	..	..	..	..	..
IgA	..	..	..	..	..	..	..	..
Not specified (IgG, IgM, or IgA)	..	..	..	..	..	..	..	..
Unclear	..	..	..	..	..	..	..	..
Populations at high risk								
Female sex workers								
Current genital infection								
NAAT	12	4877	590	8·4% (0·9–72·9)	12·9 (6·5–21·0)	602·1 (p<0·0001)	98·2% (97·6–98·6)	0·0–52·0
Culture	1	116	8	..	6·9 (3·0–13·1)	..	..	..
Other§	1	30	9	..	30·0 (14·7–49·4)	..	..	..
Overall current genital infection	14	5023	607	8·4% (0·9–72·9)	13·2 (7·2–20·7)	611·7 (p<0·0001)	97·9% (97·3–98·3)	0·0–50·9
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	4	472	364	90·0% (19·8–100)	80·9 (43·8–100·0)	209·9 (p<0·0001)	98·6% (97·7–99·1)	0·0–100·0
IgM (recent infection)	1	154	45	..	29·2 (22·2–37·1)	..	..	..
IgA	..	..	..	..	..	..	..	..
Not specified (IgG, IgM, or IgA)	1	30	11	..	36·7 (19·9–56·1)	..	..	..
Unclear	..	..	..	..	..	..	..	..
Men who have sex with men								
Current genital infection								
NAAT	12	2680	51	1·2% (0–8·8)	1·2 (0·2–2·8)	76·2 (p<0·0001)	85·6% (76·5–91·1)	0·0–9·5
Culture	..	..	..	..	..	..	..	..
Other§	..	..	..	..	..	..	..	..
Current rectal infection								
PCR	7	1506	129	6·3% (3·6–18·3)	7·7 (4·2–12·0)	40·6 (p<0·0001)	85·2% (71·5–92·3)	0·0–24·9
Overall current infection	19	4186	180	3·6% (0–18·3)	3·0 (1·2–5·4)	231·8 (p<0·0001)	92·2% (89·3–94·4)	0·0–17·9

(Table 3 continues on next page)

	Studies (n)	Samples		*C trachomatis* prevalence (median [range])	Pooled average *C trachomatis* prevalence (estimate [95% CI])	Heterogeneity measures		
		Tested	*C trachomatis* positive			*Q* (p value)*	I^2† (95% CI)	Prediction interval‡
(Continued from previous page)								
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	..	..	..	..	..	..	..	..
IgM (recent infection)	..	..	..	..	..	..	..	..
IgA	..	..	..	..	..	..	..	..
Not specified (IgG, IgM, or IgA)	..	..	..	..	..	..	..	..
Unclear	1	2531	890	..	35·2 (33·3–37·1)	..	..	..
Infertility clinic attendees								
Current genital infection								
NAAT	37	4653	539	8·0% (0–39·4)	10·2 (7·5–13·1)	310·9 (p<0·0001)	88·4% (85·0–91·0)	0·1–31·0
Culture	7	1149	176	9·5% (1·1–65·3)	14·4 (4·8–27·7)	140·8 (p<0·0001)	95·7% (93·3–97·3)	0·0–69·2
Other§	20	1844	203	10·2% (3·0–53·8)	12·3 (8·5–16·5)	112·8 (p<0·0001)	83·2% (75·1–88·6)	0·5–33·7
Overall current genital infection	64	7646	918	9·2% (0–65·3)	11·3 (9·0–13·7)	574·9 (p<0·0001)	89·0% (86·7–90·9)	0·2–33·3
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	37	3608	689	18·6% (0–85·2)	21·5 (16·3–27·2)	531·8 (p<0·0001)	93·2% (91·6–94·6)	0·2–59·7
IgM (recent infection)	17	3145	332	4·6% (0–86·7)	10·2 (5·0–16·8)	435·4 (p<0·0001)	96·3% (95·2–97·2)	0·0–47·0
IgA	6	2302	82	3·6% (0–5·0)	1·8 (0·1–4·7)	54·4 (p<0·0001)	90·8% (82·8–95·1)	0·0–16·4
Not specified (IgG, IgM, or IgA)	5	760	211	23·2% (11·1–44·4)	26·1 (17·9–35·3)	27·5 (p<0·0001)	85·4% (67·8–93·4)	2·6–61·8
Unclear	6	430	73	14·8% (3·3–33·0)	14·9 (7·0–24·8)	30·0 (p<0·0001)	83·3% (65·1–92·0)	0·0–53·3
Women with miscarriage								
Current genital infection								
NAAT	6	597	87	13·3% (1·4–22·9)	12·9 (7·4–19·5)	24·4 (p=0·0002)	79·5% (55·3–90·6)	0·1–38·9
Culture	2	112	7	10·9% (5·0–16·7)	7·1 (0·0–21·8)	2·1 (p=0·1483)	52·1% (0·0–88·0)	..
Other§	3	434	76	12·4% (7·2–25·5)	14·4 (4·9–27·6)	21·9 (p<0·0001)	90·8% (76·1–96·5)	0·0–100·0
Overall current genital infection	11	1143	170	12·4% (1·4–25·5)	12·4 (7·9–17·7)	58·0 (p<0·0001)	82·8% (70·5–89·9)	0·6–34·3
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	7	675	84	14·2% (4·1–33·3)	12·4 (6·6–19·5)	33·5 (p<0·0001)	82·1% (64·2–91·0)	0·0–39·6
IgM (recent infection)	5	352	82	21·2% (0–38·3)	21·2 (11·9–32·2)	16·2 (p=0·0028)	75·3% (39·1–89·9)	0·0–61·8
IgA	1	97	2	..	2·1 (0·3–7·3)	..	..	..
Not specified (IgG, IgM, or IgA)	2	149	13	7·3% (0–14·6)	4·7 (0·0–27·9)	16·1 (p<0·0001)	93·8% (80·0–98·1)	..
Unclear	1	84	2	..	2·3 (0·3–8·3)	..	..	..
Women with ectopic pregnancy								
Current genital infection								
NAAT	..	..	..	..	..	..	..	..
Culture	..	..	..	..	..	..	..	..
Other§	..	..	..	..	..	..	..	..
Overall current genital infection	..	..	..	..	..	..	..	..
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	2	54	20	37·5% (30·0–45·0)	37·1 (22·4–53·0)	1·4 (p=0·2418)	27·0%	..
IgM (recent infection)	1	24	1	..	4·2 (0·1–21·1)	..	..	..
IgA	..	..	..	..	..	..	..	..
Not specified (IgG, IgM, or IgA)	..	..	..	..	..	..	..	..
Unclear	..	..	..	..	..	..	..	..
Symptomatic women								
Current genital infection								
NAAT	49	14 398	1123	8·0% (0–68·0)	8·8 (6·2–11·7)	1506·7 (p<0·0001)	96·8% (96·3–97·3)	0·0–35·4
Culture	10	2951	752	12·9% (0·7–69·4)	18·9 (4·1–40·9)	1511·1 (p<0·0001)	99·4% (99·3–99·5)	0·0–97·2
Other§	31	4796	729	14·7% (0–89·3)	16·8 (11·6–22·7)	723·8 (p<0·0001)	95·9% (94·9–96·6)	0·0–55·4

(Table 3 continues on next page)

	Studies (n)	Samples		*C trachomatis* prevalence (median [range])	Pooled average *C trachomatis* prevalence (estimate [95% CI])	Heterogeneity measures		
		Tested	*C trachomatis* positive			*Q* (p value)*	I^2† (95% CI)	Prediction interval‡
(Continued from previous page)								
Overall current genital infection	90	22 145	2604	11·7% (0–89·3)	12·4 (9·4–15·7)	4323·7 (p<0·0001)	97·9% (97·7–98·1)	0·0–52·3
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	23	2377	609	18·2% (2·7–86·0)	22·7 (15·4–31·0)	454·1 (p<0·0001)	95·2% (93·8–96·2)	0·0–67·9
IgM (recent infection)	9	1042	160	3·1% (0–86·0)	13·9 (1·9–33·6)	452·7 (p<0·0001)	98·2% (97·6–98·7)	0·0–91·3
IgA	5	365	93	12·5% (3·7–59·6)	24·9 (6·6–49·6)	98·9 (p<0·0001)	96·0% (93·0–97·7)	0·0–100·0
Not specified (IgG, IgM, or IgA)	7	2530	761	15·0% (11·6–46·6)	23·5 (11·1–38·7)	346·8 (p<0·0001)	98·3% (97·6–98·4)	0·0–80·0
Unclear	6	943	83	7·7% (1·7–30·0)	8·7 (4·3–14·4)	32·2 (p<0·0001)	84·5% (67·9–92·5)	0·0–32·6
Symptomatic men								
Current genital infection								
NAAT	14	7160	726	12·2% (4·2–33·3)	13·9 (8·3–20·6)	488·7 (p<0·0001)	97·3% (96·5–98·0)	0·0–46·4
Culture	5	4744	75	9·3% (0·4–19·6)	8·7 (1·1–21·7)	147·5 (p<0·0001)	97·3% (95·6–98·3)	0·0–72·7
Other§	13	2499	355	27·6% (4·7–52·0)	26·3 (15·3–39·1)	351·7 (p<0·0001)	96·6% (95·4–97·5)	0·0–78·9
Overall current genital infection	32	14 403	1156	15·5% (0·4–52·0)	17·4 (12·5–22·8)	1628·1 (p<0·0001)	98·1% (97·8–98·4)	0·0–53·3
Anti-*C trachomatis* immunoglobulins								
IgG (ever infection)	8	831	164	14·4% (5·1–46·0)	16·9 (9·4–25·8)	69·6 (p<0·0001)	89·9% (82·6–94·2)	0·0–52·8
IgM (recent infection)	3	330	24	3·9% (2·8–12·2)	6·0 (1·4–13·0)	9·3 (p=0·0095)	78·5% (31·0–93·3)	0·0–100·0
IgA	..	..	..	..	..	..	..	..
Not specified (IgG, IgM, or IgA)	5	1596	687	46·0% (10·0–49·1)	35·6 (18·5–54·9)	143·3 (p<0·0001)	97·2% (95·4–98·3)	0·0–97·3
Unclear	8	4876	233	14·3% (1·6–76·9)	24·0 (9·2–42·8)	498·1 (p<0·0001)	98·6% (98·1–99·0)	0·0–90·3

A minimum of two studies was necessary to do a meta-analysis. The same population might have contributed different measures for both current and ever infection with *C trachomatis*. NAAT=nucleic acid amplification test. *Cochran's *Q* statistic is a measure assessing the existence of heterogeneity in effect size of *C trachomatis* prevalence across studies. †I^2 is a measure assessing the magnitude of between-study variation that is due to differences in effect size of *C trachomatis* prevalence across studies rather than chance. ‡Prediction interval is a measure estimating the 95% CI of the distribution of true effect sizes of *C trachomatis* prevalence measures. §Other assays detecting current infection such as direct fluorescence assays, Giemsa staining, and enzyme-linked immunoassays applied to genital samples.

Table 3: **Results of meta-analyses on studies reporting *Chlamydia trachomatis* prevalence in the Middle East and north Africa stratified by at-risk population and *C trachomatis* ascertainment**

of normal random effects was confirmed through normal probability plots (appendix p 43).[186] Graphical illustrations of the fitted regression line for year of publication and year of data collection are shown in the appendix (p 44). Only at-risk population, assay type, sample size, country, and sex remained associated with *C trachomatis* prevalence in a multivariable model. No evidence was found for a temporal variation in prevalence (p=0·281 for year of publication), for sampling methodology (p=0·347), or for response rate (p=0·237). This model explained 29·0% of prevalence variation.

Relative to general populations, the adjusted odds ratio (aOR) was 11·28 (95% CI 5·78–22·01) for female sex workers, 7·17 (4·05–12·68) for symptomatic men, 4·93 (1·03–23·52) for women with ectopic pregnancy, 4·16 (1·72–10·08) for men who have sex with men, 3·39 (2·41–4·77) for infertility clinic attendees, 3·47 (2·47–4·87) for symptomatic women, 2·78 (1·57–4·93) for women with miscarriage, and 1·81 (0·79–4·13) for populations at intermediate risk. Other factors associated with *C trachomatis* prevalence were women versus men (aOR 1·61, 95% CI 1·05–2·46), Pakistan versus other Middle East or north African countries (0·39, 0·22–0·69), ever infection (anti-*C trachomatis* IgG; 2·17, 1·54–3·06) and current infection prevalence using assays other than NAAT or culture versus NAAT (1·47, 1·02–2·13), and studies with higher (≥200 participants) versus lower precision (0·63, 0·48–0·83).

Discussion

We provided a comprehensive assessment of *C trachomatis* epidemiology in the Middle East and north Africa.[2,3] Unexpectedly, given this region's sexually conservative norms and low observed levels of several viral STIs,[10,11,187–189] *C trachomatis* current infection prevalence was 3% in the population at large, similar to WHO prevalence estimates for this region of about 3% in 2012[3] and about 3·5% in 2016.[190] The prevalence was also in line with WHO estimates for the Western Pacific region (about 4%) and European region (about 3%),[190] where broad *C trachomatis* control programmes, including opportunistic testing, are standard in some high-income countries,[191–193] but higher than that for South-east Asia region (about 1·5%) and lower than that for the African region (about 5%) and the region of the Americas (about 5·5%).[190] This high prevalence suggests substantial infection and disease burden that needs to be tackled through sexual health and STI-specific programmes, for both women and men. Although these findings were based on a volume of epidemiological evidence, most studies used convenience

sampling (about 90%) or had unclear response rate (>75%). Meta-regression, however, did not identify an effect for these factors on observed prevalence. A summary of this study and its results in Arabic language can be found in the appendix (p 4).

Although infection prevalence in the population at large suggests active transmission networks for *C trachomatis* and other STIs, it might not necessarily reflect prevalent sexual risk behaviours. This outcome might reflect, at least in part, poor access to and utilisation of STI services—there is very limited capacity in the Middle East and north Africa for STI prevention and treatment, not to mention *C trachomatis* screening and broader sexual health programmes. As observed elsewhere, such as in Alaskan Eskimo populations[194] and populations in South Pacific Islands,[195] poor *C trachomatis* diagnosis and specific treatment can result in unusually high prevalence,[194,196] probably because *C trachomatis* is largely asymptomatic,[4] and if untreated, shedding can persist even for years,[197] thereby increasing the potential for reinfection within couples[198] and for transmission in the population.

The high prevalence found in populations at high risk such as female sex workers, in context of evidence suggesting strong partial immunity against reinfection,[199] is consistent with the important role of commercial sex networks in infection transmission. Independent evidence supports existence of hidden pockets of high sexual-risk behaviour driving STI incidence in the Middle East and north Africa.[10,11] Among male STI patients, 77% in Kuwait[200] and 80% in Somalia[201] reported paying a female sex worker for sex, and among migrant workers in Pakistan 22% reported sex with a female sex worker.[202] Higher levels of sexual-risk behaviour and emerging HIV epidemics have been also documented among men who have sex with men, male sex workers, and male-to-female transgenders in systematic reviews.[17,203] Sexual networks, however, remain poorly investigated in the Middle East and north Africa, owing to cultural sensitivities.

The possible role of *C trachomatis* infection in poor reproductive health outcomes remains unappreciated and neglected by the public health establishment in the Middle East and north Africa, despite substantial social and economic implications for women and their families.[204,205] A main finding of this study is the high current *C trachomatis* infection prevalence in infertility clinic attendees, with odds of infection three-times higher than in the general population. By contrast, studies among infertility clinic attendees in Europe usually show that current *C trachomatis* infection is uncommon, but serological evidence of past infection, assumed to have resulted in fallopian tube scarring, is common.[206–209] This finding suggests a role for *C trachomatis* in infertility in the Middle East and north Africa. Indeed, this region appears to have the highest rate of primary infertility worldwide, which remains unexplained.[12] The Middle East and north Africa is also a region where infertility has multiple

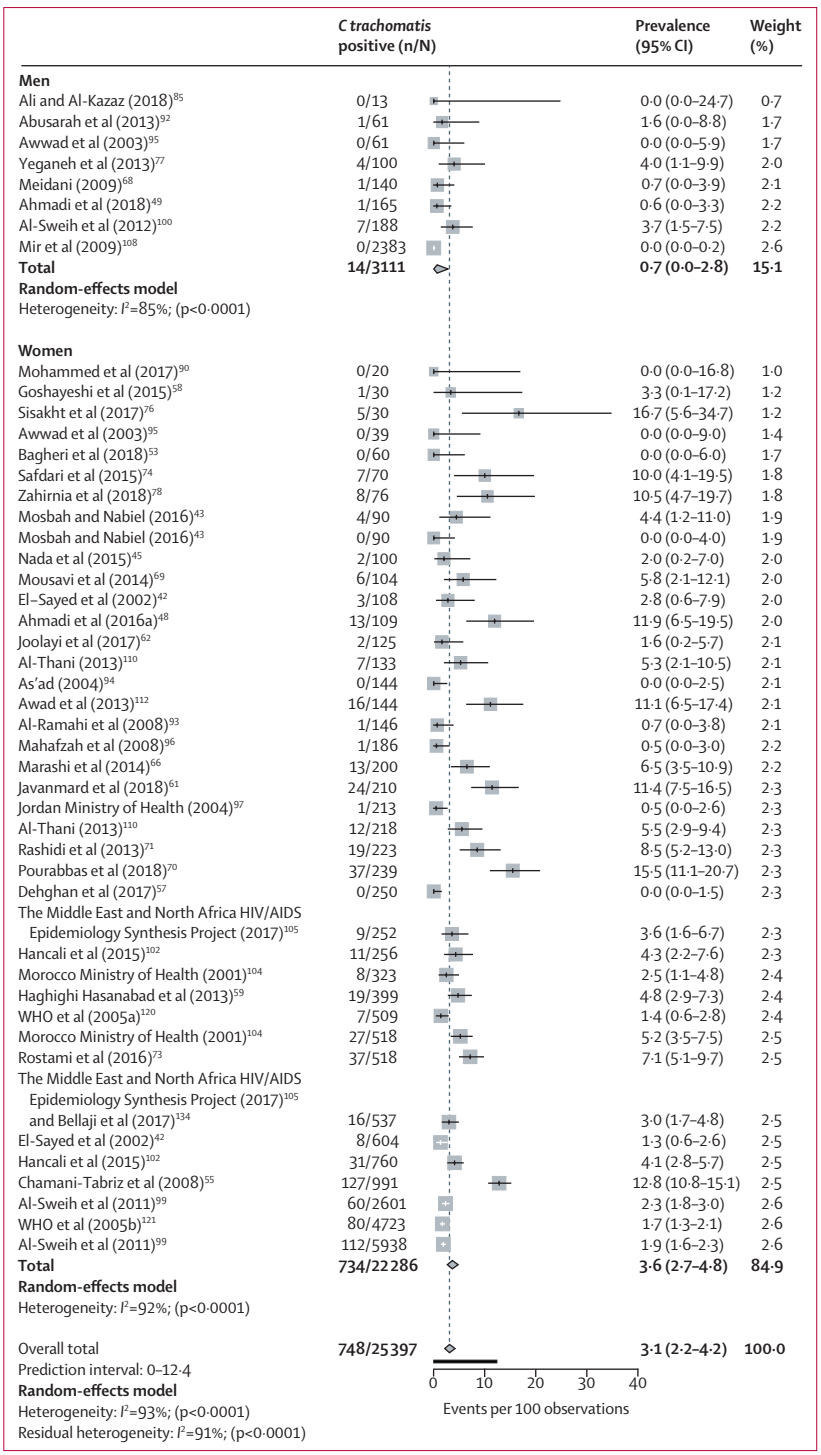

Figure 2: **Meta-analysis of studies reporting *Chlamydia trachomatis* current infection prevalence assessed using nucleic acid amplification test in the general population in the Middle East and north Africa**
Data are stratified by sex. Error bars are 95% CIs.

detrimental sociocultural consequences,[210] and where several countries have had rapidly declining fertility rates to even below replacement level.[211,212] The prevalence of current *C trachomatis* infection was also high in women

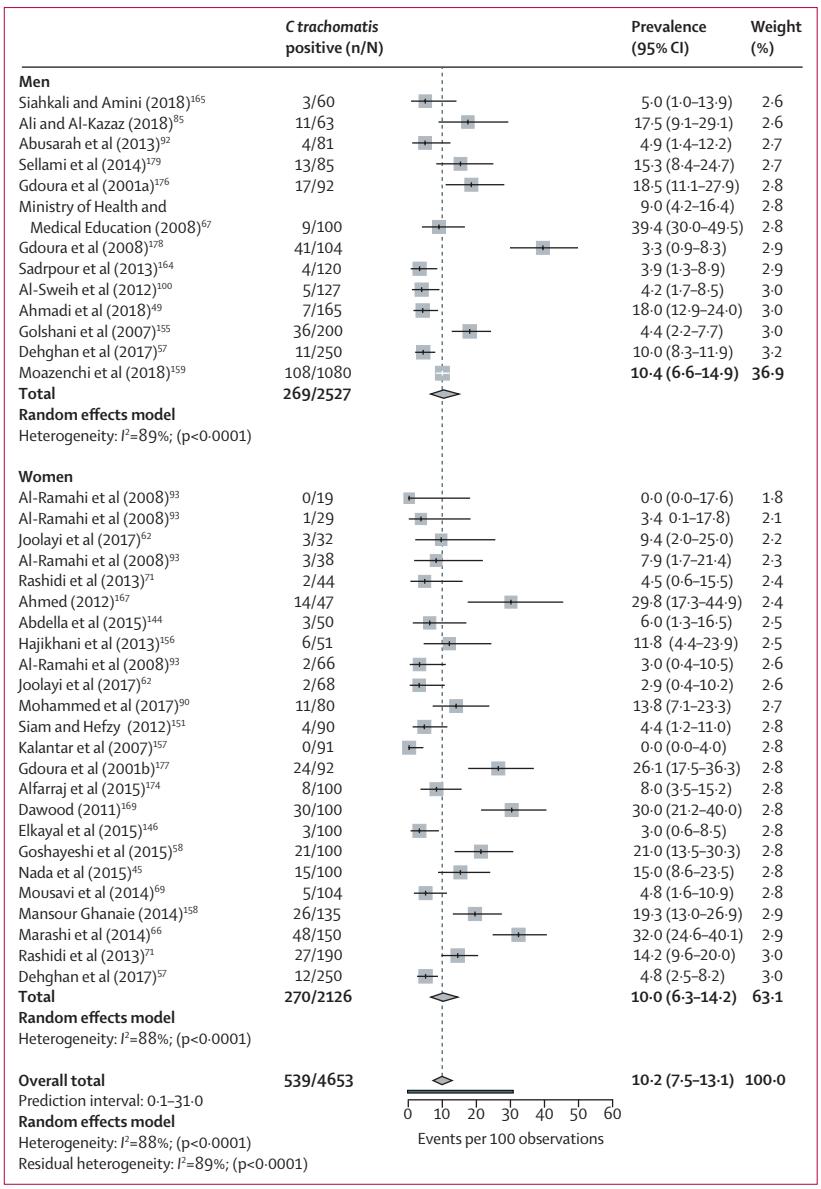

Figure 3: **Meta-analysis of studies reporting *Chlamydia trachomatis* current infection prevalence assessed using nucleic acid amplification test in infertility clinic attendees in the Middle East and north Africa**
Data are stratified by sex. Error bars are 95% CIs.

with miscarriage and in pregnant women—similar to that found in pregnant women in low-income and middle-income countries elsewhere.[213–217] This stigmatised and largely asymptomatic infection might not be visible to the public eye, but its reproductive health sequelae are visible, even if not explicitly linked to the underlying cause.

C trachomatis prevalence in women was higher than in men (two-times higher odds). This difference possibly reflects a longer duration of infection for women, considering that infection in men is more symptomatic[218] (nearly two-times higher prevalence in symptomatic men than in symptomatic women), and therefore more likely to be treated. Ever infection (anti-*C trachomatis* IgG) prevalence was two-times higher than current infection prevalence, but the epidemiological relevance of ever infection prevalence might be limited given challenges in *C trachomatis* serology interpretation.[219]

The Middle East and north Africa is burdened by *C trachomatis* infection, but the public health response remains rudimentary and far from achieving WHO's Global Health Sector Strategy on STIs.[8] Evidence for some differences in *C trachomatis* prevalence by country has been reported, but remarkably, no evidence was found for a variation in prevalence over time (1982–2018). Lingering STI stigma prevents those infected from accessing proper health care, including those most at risk. The role of screening and treatment for asymptomatic *C trachomatis* within established programmes, such as for family planning, primary health care, or HIV, needs careful consideration given the cost and uncertain effect on prevalence at modest levels of uptake.[220]

Current STI surveillance focused on inefficient routine case reporting is not capturing the reality of the transmission dynamics.[221] Although routine case reporting could be improved with more consistency and universality in reporting and emphasis on aetiological approaches,[221] its usefulness for a robust long-term evaluation of infection trends is rather limited. Sentinel surveillance of different at-risk populations should be explored, as recommended by the WHO Global Health Sector Strategy on STIs,[8] to better identify outbreaks or emerging epidemics, strategically direct resources for prevention, treatment, and control, and monitor and evaluate STI programmes.[1] The recent progress in HIV surveillance in the Middle East and north Africa, in the form of repeated rounds of HIV-integrated biobehavioural surveillance surveys,[222,223] should be extended to STIs.[221,224]

Our study has important but unavoidable limitations. Quantity and quality of available data varied by country and population, particularly for populations at high risk where most data came from only a few countries—eg, most studies of men who have sex with men were from Pakistan. No data were identified for Afghanistan, Bahrain, Libya, and Yemen. Prevalence levels might not have been strictly representative and might have been affected by publication bias, as suggested by the small-study effect observed. Studies in women with miscarriage might have included women with induced abortions; however, these were not explicitly indicated, possibly for legal reasons, as abortion is illegal in most of the Middle East and north Africa.[225,226] The wide array of diagnostics used for ascertainment might have also introduced detection bias.

Factors that might have contributed to differences in *C trachomatis* positivity rates across studies include sampling variation and potential selection bias, spatial or temporal variability in prevalence, and possibly unreported underlying comorbidities. This study did not assess other STIs that might have also contributed to infertility, pregnancy-related morbidity, and other health conditions in women with *C trachomatis* infection. Such

potential biases might have contributed to some of the unexplained heterogeneity observed in the prevalence levels. Given potential limitations in the representativeness of the prevalence measures as well as heterogeneity across studies, the calculated pooled prevalence should be interpreted as a pooled average, rather than strictly

	Studies (n)	Samples (n)	Univariable analyses			Variance explained R^2	Multivariable analysis		
			OR (95% CI)	p value	LR test p value*		Adjusted OR (95% CI)	p value	LR test p value†
At-risk population									
General populations	137	168 302	1·00 (ref)	..	<0·0001	19·0%	1·00 (ref)	..	<0·0001
Populations at intermediate risk	14	4164	0·70 (0·32–1·54)	0·374	..	..	1·81 (0·79–4·13)	0·157	..
Female sex workers	20	5679	8·99 (4·57–17·71)	<0·0001	..	..	11·28 (5·78–22·01)	<0·0001	..
Men who have sex with men	20	6717	0·83 (0·42–1·64)	0·591	..	..	4·16 (1·72–10·08)	0·002	..
Infertility clinic attendees	135	17 891	3·77 (2·67–5·31)	<0·0001	..	..	3·39 (2·41–4·77)	<0·0001	..
Women with miscarriage	27	2500	3·53 (1·94–6·40)	<0·0001	..	..	2·78 (1·57–4·93)	0·001	..
Women with ectopic pregnancy	3	78	8·25 (1·58–43·08)	0·012	..	..	4·93 (1·03–23·52)	0·045	..
Symptomatic women	140	29 402	3·74 (2·66–5·26)	<0·0001	..	..	3·47 (2·47–4·87)	<0·0001	..
Symptomatic men	56	22 036	5·76 (3·68–9·03)	<0·0001	..	..	7·17 (4·05–12·68)	<0·0001	..
Assay type									
NAAT (current infection)	197	64 083	1·00 (ref)	..	<0·0001	7·1%	1·00 (ref)	..	<0·0001
Culture (current infection)	29	13 536	1·92 (1·05–3·50)	0·034	..	..	1·10 (0·62–1·95)	0·742	..
Other (current infection)‡	92	137 924	1·90 (1·30–2·79)	0·001	..	..	1·47 (1·02–2·13)	0·041	..
Anti-*C trachomatis* immunoglobulins§									
IgG (ever infection)	117	14 935	2·99 (2·10–4·26)	<0·0001	..	..	2·17 (1·54–3·06)	<0·0001	..
IgM (recent infection)	49	7890	1·17 (0·72–1·90)	0·517	..	..	0·90 (0·57–1·40)	0·627	..
IgA	16	3141	0·92 (0·42–2·02)	0·836	..	..	0·78 (0·39–1·56)	0·481	..
Not specified (IgG, IgM, or IgA)	29	6146	2·81 (1·54–5·13)	0·001	..	..	2·25 (1·28–3·97)	0·005	..
Unclear	23	9114	2·53 (1·30–4·94)	0·007	..	..	1·49 (0·81–2·75)	0·200	..
Sampling methodology¶									
Non-probability-based sampling	495	227 208	1·00 (ref)	..	<0·0001	3·5%	1·00 (ref)	..	0·347
Probability-based sampling	57	29 561	0·37 (0·24–0·56)	<0·0001	..	..	0·80 (0·50–1·27)	0·347	..
Sample size									
<200	386	32 782	1·00 (ref)	..	<0·0001	6·0%	1·00 (ref)	..	0·001
≥200	166	223 987	0·42 (0·32–0·56)	<0·0001	..	..	0·63 (0·48–0·83)	0·001	..
Response rate									
≥80%	112	38 732	1·00 (ref)	..	0·187	0·1%	1·00 (ref)	..	0·237
<80% or unclear	440	218 037	0·80 (0·57–1·12)	0·187	..	..	0·83 (0·61–1·13)	0·237	..
Year of publication‖	552	256 769	0·96 (0·95–0·98)	<0·0001	<0·0001	4·4%	0·99 (0·98–1·01)	0·281	0·281
Year of data collection	552	256 769	0·96 (0·95–0·98)	<0·0001	<0·0001	4·2%	..	..	..
Country									
Other Middle East or north African countries	245	189 529	1·00 (ref)	..	<0·0001	5·2%	1·00 (ref)	..	0·013
Egypt	89	7434	1·58 (1·08–2·31)	0·018	..	..	1·05 (0·73–1·51)	0·774	..
Iran	176	38 647	0·80 (0·59–1·08)	0·145	..	..	0·90 (0·68–1·19)	0·472	..
Pakistan	42	21 159	0·31 (0·19–0·52)	<0·0001	..	..	0·39 (0·22–0·69)	0·002	..
Sex									
Men	133	42 393	1·00 (ref)	..	0·131	0·2%	1·00 (ref)	..	0·029
Women	419	214 376	1·27 (0·93–1·74)	0·131	..	..	1·61 (1·05–2·46)	0·029	..

Adjusted R^2 in the final multivariable model was 29·0%. LR=likelihood ratio. NAAT=nucleic acid amplification test. OR=Odds ratio. *Predictors with p≤0·2 in the univariable model were considered significant. †Predictors with p≤0·05 in the multivariable model were considered significant. ‡Other assays detecting current infection such as direct fluorescence assays, Giemsa staining, and enzyme-linked immunoassays applied to genital samples. §Includes assays such as enzyme-linked immunoassay and micro-immunofluorescence. ¶Non-probability sampling refers to a sampling method in which the data collection process does not allow individuals to have equal chance of being selected; an example is convenience sampling for which individuals are selected on the basis of ease of accessibility (first-come first-served basis).[127,128] Probability-based sampling refers to a sampling method in which data collection process is based on a random selection of study participants; an example is random sampling from a sampling frame.[128] Another example of probability-based sampling is respondent-driven sampling, which is a sampling method specifically designed to sample hard-to-reach populations and is based on chain referral with the probability of selection calculated at each step in the network to produce adjusted prevalence estimates.[129] ‖Only year of publication was considered for the multivariable meta-regression analysis because of collinearity with year of data collection.

Table 4: **Results of meta-regressions to identify associations and sources of between-study heterogeneity for *Chlamydia trachomatis* prevalence in the Middle East and north Africa**

an estimate of the mean prevalence in the considered population or subpopulation.

In conclusion, *C trachomatis* current infection prevalence in the population at large in the Middle East and north Africa is at 3%, similar to other regions, but higher than expected given these countries' sexually conservative norms. The high prevalence (>10%) in infertility clinic attendees and in women with miscarriage, provides suggestive evidence for the potential role of *C trachomatis* in poor reproductive outcomes in the Middle East and north Africa. In the context of very limited programming for sexual health and STIs, our findings highlight an important, yet neglected and poorly recognised infection and disease burden, despite the social and economic impact. There is an urgent need for targeted and culturally appropriate programmes promoting sexual health for different at-risk populations. Tackling this infection with appropriate interventions is essential to control disease sequelae, to address the WHO Global Health Sector Strategy on STIs,[8] and to accomplish key health Sustainable Development Goals.

Contributors

AS contributed to the study design, did the systematic searches of the literature, selection of studies for inclusion, and the data extraction and data analyses. HC contributed to the study design, double extracted the data, updated the systematic review, and did the data analyses. AS and HC wrote the first draft of the paper. JGH contributed to identification of unpublished data. NL contributed to the data extraction, analyses, and drafting of the Article. LJA-R conceived and led the design of the study, data extraction, data analyses, and drafting of the Article. All authors contributed to discussion and interpretation of the results and to the writing of the manuscript. All authors have read and approved the final manuscript.

Declaration of interests

We declare no competing interests.

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